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LIGHT AND THE A-BODY *

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In a previous article, entitled "Light and the Antirachitic Factor," Frans Faber and I [1] maintained that the so-called antirachitic factor was not specific, because in addition to the antirachitic effect it also had an activating influence on other functions, and, moreover, that it could not be a vitamin but must be the energy of the ultraviolet rays.

While the antirachitic factor, according to our conception, is not a substance, there is no doubt that the A-body is an actual substance. J. C. Drummond and his collaborators have shown that the A-body is an organic substance which acts as such and not indirectly as a ferment. The A-body does not belong to the lipoid bodies, which I presumed when I first discussed this substance in 1914 and 1916, but, according to a statement of Drummond, the investigator who has gone most deeply into its chemical constitution, it is probably a special alcohol or aldehyde.

We further know that the A-body is formed by light in the green —the creating—parts of the plant. Drummond and Katharine H. Coward,[2] in a series of accurate experiments, have proved that the production is independent of chlorophyll, and that neither oxygen nor carbonic acid need be present in the surrounding air; that it is produced not only when the plant is exposed to sunlight but also by the carbon arc light; that the light rays are the active ones, the ultraviolet rays being inactive in this respect.

Thus, while it is clear that light produces the A-body in plants, it is doubtful whether it has a similar action on the animal organism, permitting exposure to sunlight to wholly or partly replace the administration of the A-body.

EXPERIMENTAL DATA

Those authors who regard the A-body and the antirachitic factor as closely related vitamins were prompted to investigate whether light

* Received for publication, Oct. 10, 1925.

* From the Children's Department of Rigshospitalet, University of Copenhagen.

1. Bloch, C. E., and Faber, Frans: Light and the Antirachitic Factor, Am. J. Dis. Child. **30**:504 (Oct.) 1925.

2. Drummond, J. C., and Coward, K. H.: Biochem. J. **26**:482, 1922.

had the same curative effect on the experimental A-body deficiency diseases as on experimental (and clinical) rickets. Experiments on this point were made almost simultaneously by E. Margaret Hume [3] (Lister Institute), and by Goldblatt and Soames [4] with negative results; exposure to ultraviolet light could not take the place of the A-body. On the contrary, it had a harmful action, for the ultraviolet rays stimulated the growth of the young rats, which rapidly exhausted the animal's depôt of A-body so that xerophthalmia in its most serious form occurred early, and the animals succumbed long before the controls, which had received the same diet poor in A-body but which had not been exposed to ultraviolet rays.

Powers, Park and Simmonds [5] have extended the experiments to include ordinary daylight in a closed laboratory, complete darkness and sunlight, as well as ultraviolet light. Their experiments gave the same results as the previous ones, except that the animals which were exposed to sunlight behaved differently from the other groups. It was found that the "sunlight animals" grew to some extent, but the sunlight could not further the growth in the same way as when the animals received the A-body factor. Furthermore, with a single exception, they did not develop xerophthalmia before all the animals from the other groups were dead from A-body deficiency. One of the "sunlight animals" had practically no xerophthalmia, while in the others it was relatively slight and showed a tendency to heal spontaneously with further sunlight treatment.

These sunlight experiments did not all agree, and, as the authors admit, they are not clear experiments, because the "sunlight animals," besides having been exposed to sunlight have also lived in the open air and have been subjected to large temperature variations. Provided that the variable results of these experiments are not due to chance—not all young rats get xerophthalmia even if they are kept on a diet free from the A-body factor—they indicate that sunlight, unlike ultraviolet light, can, in some way or other, serve instead of the administration of the A-body.

From the Lister Institute a similar experiment was previously reported by E. Margaret Hume.[6] She investigated whether the amount of A-body in cow's milk was increased when the cow was exposed to sunlight. Both this experiment and a later one by Ethel M. Luce [7] gave a negative result. The milk's growth-promoting power (that is

3. Hume, E. M.: Lancet **2**:1318 (Dec. 23) 1922.
4. Goldblatt, H., and Soames, K. M.: Lancet **2**:1321 (Dec. 23) 1922.
5. Powers, G. F.; Park, E. A., and Simmonds, N.: J. Biol. Chem. **55**:575 (April) 1923.
6. Hume, E. M.: Studies of Rickets in Vienna, 1919-1922. Report to the Medical Research Council, London, 1923, p. 140.
7. Luce, E. M.: Biochem. J. **18**:1279, 1924.

its A-body content) was unchanged; it was the same whether the cow was kept in a dark stall or was exposed to sunlight in the open air. But the milk's antirachitic effect was considerably increased when the cow was exposed to sunlight. This agrees well with all previous clinical and experimental investigations, all of which show that light, especially the ultraviolet rays, has an antirachitic action. On my assumption that the antirachitic factor and the ultraviolet radiation energy are identical, this experiment indicates that the energy which the cow has absorbed from the light passes over into its milk; the milk, being charged with this energy, acquires stronger antirachitic properties.

While, therefore, there are a number of facts which show that ultraviolet light can have an activating but not a specific effect on the animal organism, the experiments, here referred to, indicate that we do not yet know with certainty whether light rays, that part of the light which excites the production of the A-body in plants, acts in the same way in the animal organism.

No information has hitherto been forthcoming from the clinic as to whether light can take the place of the administration of the A-body. We only know that the A-body deficiency diseases in children, particularly that characteristic symptom, xerophthalmia, cease almost entirely in the summer, when sunlight is strongest, but, as has been previously pointed out,[8] it is probable that this periodic occurrence is not directly due to the light but is connected with the different growth periods.

On account of the danger of threatening blindness, clinical xerophthalmia is such a serious disease that new treatment cannot be tried. As soon as the diagnosis has been made, one must apply the treatment which is known to be effective, namely, the immediate introduction of the A-body into the organism, per os or subcutaneously. Last autumn, however, two children, brother and sister, were admitted to the State Hospital with xerophthalmia. These cases were unusual in several respects, partly because they were relapses of xerophthalmia, partly on account of the season—xerophthalmia in children over 1 year old seldom occurs in the autumn—but chiefly because one of the children could only absorb an extremely small amount of the A-body from the digestive canal; although this boy took large doses of cod liver oil in a preparation which we knew was active, the xerophthalmia persisted practically unchanged.

As, moreover, the children were only slightly affected and as they were under constant observation at the hospital, I thought that an experiment with light treatment was justifiable before proceeding to give subcutaneous injections of the A-body.

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8. Bloch, C. E.: Blindness and Other Diseases in Children Arising from Deficient Nutrition, Am. J. Dis. Child. **27**:139 (Feb.) 1924.

REPORT OF CASES

CASE 1.—*History.*—P. T., a boy, was born June 23, 1915. He was admitted to the hospital Nov. 1, 1924, and discharged March 30, 1925.

The patient was sent to the State Hospital by the school physician in March, 1924, because of bad eyesight. Xerosis conjunctivae was diagnosed in the ophthalmic department. Cod liver oil and fresh milk were ordered. As the disease proved refractory to this treatment, he received cod liver oil subcutaneously in June. The xerosis then disappeared entirely. The boy was in the country all the summer and was in good health.

During the autumn he had periodic attacks of diarrhea, which he was said to have had repeatedly before, especially in the course of the last year or two. In association with this, the eye complaint became worse, and so he was admitted to hospital.

This patient came from a poor home, where the father and mother were at work all day, and the children were, therefore, left to themselves. When the mother came home at night they got their dinner. They never had milk, hardly ever butter or eggs, and only seldom food made with milk.

The patient had the appearance of being neglected and there were signs of previous rickets. On both conjunctivae bulbi there was extensive xerosis with Bitôt's spots. There was marked hemeralopia.

A gastric test meal disclosed achylia gastrica. Throughout the patient's stay in hospital a test meal was given once every month, with the same result each time.

While in hospital the motions rapidly became apparently normal. The fat content, determined by extraction, showed that the absorption of fat was normal. An examination for bile pigments showed nothing abnormal, nor was there anything wrong on examining the blood and the urine. The Wassermann reaction and Pirquet's reaction were negative. A roengten-ray examination of the osseous system showed nothing abnormal, particularly no osteoporosis or rickets.

November 1, a diet rich in A-body was given, especially in the form of milk. November 13, the xerosis and hemeralopia were practically unchanged. A diet deficient in A-body was ordered, and carbon arc light baths, beginning with half an hour and rising to two hours every other day, were given. December 29, the light baths were discontinued. The xerosis was almost the same. There was a white, fatty film on some of the xerotic spots. On examination with Tscherning's photometric glass, rather advanced hemeralopia was detected.

The diet deficient in A-body was continued. Jan. 29, 1925, there was no marked change and the xerosis and hemeralopia were as before. A diet rich in A-body, and 15 c.c. daily of cod liver oil and malt in equal parts, were ordered.

On March 3, the xerosis and hemeralopia were still present but were perhaps a little less pronounced.

On March 9, 0.5 c.c. of concentrated A-body preparation was given intramuscularly; on March 11, 0.7 c.c.; on March 13, 0.75 c.c.; and on March 16, 0.8 c.c. were given. On March 17, the night blindness had disappeared (report from the ophthalmic department). The xerosis had nearly disappeared.

On March 16, 2 c.c. of cod liver oil was given subcutaneously. Some infiltration, tenderness and redness appeared at the site of the injection, but passed away spontaneously. There was no reaction at the sites of the A-body injections.

On March 30, the patient was transferred to the Coast Hospital at Refsnaes He was treated here with full diet containing much green vegetables and fresh milk. He had a fresh air cure, with sea baths and sun baths, and was well during the whole of his stay here.

The patient was discharged from the Coast Hospital on June 22. He was examined on June 26 at the State Hospital, at which time he was sunburnt and in a good state of nutrition. The xerosis and hemeralopia had returned and were just as bad as when he was admitted to the State Hospital on Nov. 1, 1924.

The patient's weight in grams was as follows: Nov. 1, 1924, 23,000; November 10, 25,300; November 20, 26,000; November 30, 25,700; December 10, 26,200; December 20, 27,200; December 30, 26,900; Jan. 10, 1925, 27,000; January 20, 27,500; January 30, 27,300; February 10, 28,600; February 20, 27,900; February 29, 29,300; March 10, 29,300; March 20, 29,900; March 30, 29,500, and June 26, 29,600.

The height of the patient in centimeters was as follows: Nov. 1, 1924, 121.5; November 10, 123; Jan. 5, 1925, 123.5; January 28, 124; March 29, 126; June 26, 127. The height was measured in the standing position and after at least twelve hours' rest in bed, except on Nov. 1, 1924, and June 26, 1925, when the patient had been up for a long time previously.

CASE 2.—*History.*—E. T., a girl, born Dec. 13, 1916, was admitted to hospital Nov. 28, 1924, and was discharged Feb. 15, 1925.

The eye disease was discovered in the ophthalmic department in April, 1924, when the patient was called up for examination on account of her brother's disease (Case 1). Slight xerosis of the conjunctiva of both eyes was then found. The xerosis quickly disappeared on a diet of cod liver oil and milk. In the autumn, the patient developed long-continued febrile angina, during which a recurrence of the eye disease occurred, and the child was, therefore, admitted to hospital.

The food and care she received had been the same as in the case of her brother. This patient was small, rather thin, well proportioned and had a good color.

Slight xerosis of both eyes was present and she had definite hemeralopia Tonsillitis was also present. The stomach secretions and motions were normal. On further examination, nothing particular was found.

December 3, after the angina disappeared there were still remains of xerosis on both conjunctivae bulbi. A diet deficient in A-body and carbon arc light baths for half an hour rising to two hours every other day, were ordered.

December 31, the light baths were discontinued.

Jan. 2, 1925, on examination with Tscherning's photometric glass, definite but slight hemeralopia was demonstrated (report from the ophthalmic department). There was still slight xerosis present and the diet deficient in A-body was continued.

January 29, the xerosis was almost unchanged but there was a trace of hemeralopia. A diet rich in A-body was given, and 1 tablespoonful daily of cod liver oil and malt in equal parts were also given.

February 12, the xerosis had disappeared. On examination with Tscherning's glass, no hemeralopia was found (ophthalmic department).

The patient's weight in grams was as follows: Nov. 30, 1924, 20,100; December 10, 21,400; December 20, 22,000; December 30, 22,100; Jan. 10, 1925, 22,600; January 20, 23,000; January 30, 22,600; February 15, 23,100.

Her height in centimeters was as follows: November 28, 119; January 5, 120.5; February 15, 121.5. The measurements were taken in the standing position after at least twelve hours' rest in bed, except on November 28, when the patient was up for several hours previously.

RESULTS

Both of these children had xerophthalmia, and that it was due to the organism's lack of A-body follows clearly from the fact that the xerosis disappeared as soon as this want was made good, in the girl by giving her an abundant supply of A-body in her food, and in the boy by intramuscular injections of A-body.

The clinical histories show that deficient nutrition was the chief cause of the disease. The children perhaps had received enough to eat, but the composition of the food was unsatisfactory for a long time owing to the absence of fresh milk, milk foods and green vegetables. When

the xerophthalmia in the girl returned in the autumn, it was due to the febrile disease.

In the case of the boy the further abnormality was found, that the absorption of A-body from the digestive canal was poor. It is hardly possible to explain in any other way that a diet rich in A-body, with plenty of fresh milk and cod liver oil should have had practically no effect on the xerophthalmia. In this case there were no signs of liver disease, as there were in the cases I [9] have previously described, in which xerophthalmia was due to deficient absorption of A-body; even the absorption of fat from the intestine was about normal.

The diminished amount of gastric secretion will hardly account for this abnormality either. Achylia gastrica is fairly frequently met with in childhood, and by itself, scarcely gives rise to defective absorption of A-body. On the other hand, the achylia gastrica which was present all the time the child was in the hospital, taken in conjunction with the frequently recurring diarrhea, indicates that there must have been some disease of the digestive organs, but it has not yet been possible to elucidate its exact nature.

As soon as the children had overcome the acute diseases—a period of diarrhea in the boy, and of febrile angina in the girl—they were both put on a diet deficient in A-body. At this time the boy had severe xerosis of the conjunctiva and the girl slight xerosis.

The diet deficient in A-body consisted chiefly of carbohydrates (oatmeal, barley and rice pudding, bread, plenty of sugar, malt soup, jam, potatoes), as well as vegetable margarine, lean meat and fish, fruit and from 0.25 to 0.5 liters of buttermilk daily. The children ate their food with a good appetite and put on weight.

Simultaneously with this dieting, universal light baths by Finsen's method were started. The source of the light was two 75 ampere carbon arc lamps, which were brought as near to the children as possible. They were kept in the light bath for two hours every other day. This treatment of the boy started on November 14 and ended on December 29. He received seventeen light baths, comprising a total of about thirty-two hours. The treatment of the girl started on December 4 and ended on December 20. She received eleven light baths, comprising a total of twenty hours. The children tolerated the light baths well. The skin became pigmented rapidly.

The xerosis remained unchanged the whole time. There were days when it seemed to be less marked, but this was due to the xerosis being partly hidden by the sterile vaseline which had been dropped into the eyes to relieve the soreness. If the vaseline was wiped away, it could be seen

9. Bloch, C. E.: Further Clinical Investigations Into the Diseases Arising in Consequence of a Deficiency in the Fat-Soluble A Factor, Am. J. Dis. Child. **28**:659 (Dec.) 1924.

that the xerosis was unchanged. An examination of the nightblindness, moreover, with Tscherning's photometric glass, showed that hemeralopia was still present.

Exposure to the carbon arc light under the given conditions had, therefore, not succeeded in curing the xerophthalmia; the A-body deficiency of the organism was unaltered. But the condition had not grown any worse. Was this due to the light, or had the minute amount of A-body in the food been sufficient to prevent the xerosis from spreading?

To clear up this point, the same diet, deficient in A-body, was continued for another month after the light baths were stopped. It could not be continued longer because the children became tired of the food. They lost their appetites, one result of which was that the increase in weight ceased.

The xerosis and hemeralopia remained practically unchanged during this month also. This shows the A-body in the food was sufficient to cover the consumption, and that the light was of no importance from this point of view.

There is, thus, a very considerable difference between the effect of light on rickets, tetany and the diseases discussed in the earlier paper, and on the diseases caused by A-body deficiency. In rickets and tetany, less than one hour's radiation is adequate. The effect manifests itself almost immediately and persists afterward. It is as if the organism—in the same way as an accumulator becomes charged with electricity—became recharged by the radiation with this special radiant energy, which then sets the organism's arrested phosphorus and calcium regulation in motion, and keeps it going. On the other hand, from twenty to thirty hours' radiation with the carbon arc light is completely ineffective in the absence of the A-body.

After the children had lived on the diet deficient in A-body for about two months, it was changed to full diet (plenty of milk food, fresh milk and eggs), and from 5 to 10 gm. of cod liver oil were given daily.

The girl reacted quickly to this, the xerosis and hemeralopia disappearing in a few days, with resultant recovery.

The boy's appetite and spirits were also improved, he again increased in weight; if anything, the xerosis diminished slightly, but even after a lapse of forty days the xerosis and hemeralopia were still very pronounced. That this was due to defective absorption from the digestive canal is clear from the following. Three intramuscular injections, comprising altogether 2.75 c.c. of a concentrated A-body solution (a cod liver oil preparation made by "Lovens" Medicinalfabrik, containing from twenty or thirty times as much A-body as cod liver oil itself does), were given in the course of seven days, with the result that the xerosis and hemeralopia practically entirely disappeared.

The boy was now apparently healthy. He was transferred for convalescence to the Coast Hospital at Refsnaes (Dr. Rolf Hertz), one of the resorts in this country where the sunlight is most intense, and where the sanatorium cure with sun baths and the fresh air treatment is organized on splendid lines. He also received abundant nourishment, of which fresh milk and green vegetables were the main constituents. He was at the Coast Hospital for the whole of May and the greater part of June, in both of which months there were many sunny days, and he was apparently well throughout his stay.

When he returned to the State Hospital on June 26, he had a healthy, sunburnt appearance but the xerosis had returned; both the xerosis of the conjunctiva and the hemeralopia were just as bad as ever. Sunlight and the fresh air cure, therefore, could not make up for the deficient absorption of the A-body, and prevent xerophthalmia.

COMMENT

The objections to these clinical investigations, as compared with the corresponding experimental ones, are partly that they only lasted a short time and partly that a diet more devoid of A-body was not given.

The latter difficulty could not be surmounted because such a diet would have been hard to prepare, and because the children would not have eaten it with a good appetite, but particularly on account of the danger involved in giving children attacked by xerophthalmia a diet which contained no A-body at all.

The course pursued by the disease showed that the diet was poor enough in A-body for the xerophthalmia to continue, and more than this was not needed.

On the other hand, it was an advantage in these clinical investigations that the xerophthalmia was present when the treatment with the carbon arc light was begun, and also that the same persons were observed under the same conditions, with and without light treatment. These advantages are so great that they entirely counterbalance the defects.

CONCLUSIONS

Neither exposure to carbon arc light nor to sunlight cure xerophthalmia.

Light cannot replace the A-body or supply it to the animal organism.

On the other hand, it follows from the investigations reported in the first section, that in addition to its hitherto recognized reaction, light is indispensable to the animal organism, in that the radiant energy of ultraviolet light is essential to various functions.

This energy is absorbed by the organism partly by direct radiation and partly through articles of diet (that is, cod liver oil, the yolk of eggs, and, to some extent, milk) which are charged with it.

THE RESPIRATORY METABOLISM IN INFANCY AND IN CHILDHOOD

I. BASAL METABOLISM OF CHILDREN *

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The main purpose of this first communication is to describe the apparatus and technic for measuring the respiratory exchange of children, in investigations that are to be reported subsequently.

During the course of these studies, we had occasion to determine the basal metabolism of seven children. In view of the paucity of data on this subject, it seems of sufficient interest to include the results. In constructing their standard smoothed curves for the minimal heat production of normal boys and girls from birth to puberty, Benedict and Talbot [1] plotted determinations on eleven children between the ages of 6 and 7 years, and on ten children between the ages of 10 and 11 years. Reports from other laboratories on the basal metabolism of children of similar ages are also meager.

APPARATUS AND TECHNIC

The calorimeter room is situated in a corner of the children's ward. It has a floor space of approximately 125 square feet, and is sufficiently large to hold the respiration chamber and all the accessory apparatus without interfering with the movements of the two observers during experiments. By means of two windows, a door and a heater, a uniform room temperature may be maintained. It rarely varies more than 1 C. during individual observations. The range of room temperature throughout the entire series of experiments was between 20 and 25 C.

The apparatus includes the Benedict "Cot Chamber," ventilated by the Benedict "Universal Respiration Apparatus." [2] Both units are slightly altered in the following manner:

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* Received for publication, Nov. 10, 1925.

* From the Department of Pediatrics, Cornell University Medical College, and the New York Nursery and Child's Hospital.

1. Benedict, F. G.: Energy Requirements of Children from Birth to Puberty, Boston M. & S. J. **181**:107 (July) 1919. Benedict, F. G., and Talbot, F. B.: Metabolism and Growth from Birth to Puberty, Carnegie Inst. Wash., Pub. No. 302, 1921.

2. Benedict, F. G., and Tompkins, E. H.: Respiratory Exchange, with a Description of a Respiration Apparatus for Clinical Use, Boston M. & S. J. **174**: 857, 898, 939 (June) 1916.

The absorption system is modified, so as to enable the measurement of the water as well as of the carbon dioxid eliminated by the subject for each period of the observation. This is accomplished by inserting two Williams' bottles, containing concentrated sulphuric acid, in the alternate trains in front of the carbon dioxid absorbers. The gain in weight corrected for changes in the moisture content of the chamber measures the water given off by the subject during the period. Two-liter bottles replace the smaller ones used in the original apparatus of Benedict.[2] A sulphuric acid bottle of this size efficiently takes up the moisture given off by the soda lime during the absorption of carbon dioxid. This was demonstrated by blowing carbon dioxid gas through a second sulphuric acid bottle inserted in the train after the carbon dioxid absorbers. The second bottle did not increase in weight, even when the soda lime and first sulphuric acid bottles gained over 4 gm. Additional evidence of the efficiency of the carbon dioxid absorbers is shown by the close agreement in the alcohol checks between actually found and theoretic carbon dioxid (Table 1). This is not in accord with the observation of Murlin,[3] who used 1 liter bottles in his work with infants. He found it necessary to add a phosphorus pentoxid bottle to the train to remove the last traces of moisture given off by the soda lime.

The cot chamber is rigidly constructed of 16 ounce copper, tinned on the inner surface. It is 156 cm. long and 52 cm. wide on the inside. The height at the head end is 44 cm. This measurement is reduced to 32 cm. at the foot by the gradual downward slope of the cover. The chamber accommodates children of normal size from 4 to 12 years of age. Its capacity, which ordinarily is 345 liters, may be increased to 376 liters by resting the cover on stirrups suspended in the oil seal. An oil rather than a water seal is used, to prevent evaporation of water from this source.

A hair hygrometer placed just beneath the window of the chamber records the relative humidity. The moisture in the system is maintained nearly constant during observations by regulating the flow of air through the chamber. The ventilation is, however, always returned to the initial rate fifteen minutes before the end of each period, during the last five or ten minutes of which residual samples of air are withdrawn for analysis. The relative humidity of the chamber is maintained at close to atmospheric humidity, which throughout these observations ranged from 41 to 50 per cent. The method also controls the concentration of carbon dioxid of the air in the chamber, which in these observations never exceeded 1 per cent.

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3. Murlin, J. R.; Conklin, R. E., and Marsh, M. E.: Energy Metabolism of Normal New-Born Babies, with Special Reference to the Influence of Food and of Crying, Am. J. Dis. Child. **29**:1 (Jan.) 1925.

The temperature of the chamber is controlled by evaporating water from the surface by means of an electric fan, after the method of Benedict and Tompkins.[2] Four mercurial thermometers are inserted to different depths at various places in the cover. They are read to 0.01 F. We consider the mean temperature of the chamber to be the average of the four thermometer readings. Since mercurial thermometers do not register the temperature of the surrounding air immediately, readings are recorded only after the thermometers have attained an approximate equilibrium. Preliminary periods, therefore, are prolonged until the rate of evaporation is found which maintains a uniform temperature. The rate thereafter is varied as little as possible. For the same reason, children are kept very quiet or asleep during the twenty minutes before the end of each period. These precautions are considered important factors in the technic, especially in observations during which the patient is active for part of each period. By attending strictly to these details, we believe that the error due to the thermometer lag is obviated.

The frame of the calorimeter bed is made of stained wood. A fish net with a 2-inch mesh is stretched tightly across the top of the frame.[4] Over the net are placed a thin sheet and small pillow on which the children, dressed lightly, recline. They all state that this bed is comfortable, and, in fact, one child remained on it for five hours without discomfort.

Activity of the subject is recorded directly on a smoked drum by means of a tambour and a spiral pneumograph stretched obliquely beneath the bed.[5] It is further checked by direct observation of the subject through the window, and during residual periods the fall of the spirometer bell is noted. Since the spirometer falls steadily only when the patient is quiet, any rise or irregularity in its descent indicates that the child is moving. Observations are accepted as satisfactory only when the patient remains quiet during residual periods. The cardiac rate is counted every ten to fifteen minutes, according to standard technic.[2]

Air enters the chamber beneath the cover at the head end, and is withdrawn through a perforated pipe on the floor at the foot of the chamber. We found, after numerous trials, that the air is effectively circulated by this means and that a fan is unnecessary. The usual rate of ventilation in these observations was approximately 35 liters per minute.

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4. Soderstrom, G. F.; Meyer, A. L., and Du Bois, E. F.: Clinical Calorimetry. XI. A Comparison of the Metabolism of Men Flat in Bed and Sitting in a Steamer Chair, Arch. Int. Med. **17**:872 (June) 1916.

5. Benedict, F. G.: Methoden zur Bestimmung des Gaswechsels bei Tieren und Menschen, Abderhalden's Handbuch der Biologischen Arbeitsmethoden, No. 142, Sect. 4, p. 474, 1924.

Oxygen is admitted by hand from a small, air-tight cylinder. A delicate regulator permits a small, easily controlled flow. The rate is so regulated that the volume of the system remains practically constant throughout the experiment, except during residual periods when no oxygen is admitted. At the end of each experimental period, the system is restored to the original volume by adding oxygen directly to the spirometer. The cylinder is weighed at the beginning and end of each period. The difference, corrected for changes in temperature, barometric pressure and in the composition of the air in the chamber measures the oxygen consumption. Pressure variations are recorded by an accurate barometer, which is read to 0.01 mm. Changes in the composition of the chamber air are determined by analyzing ten-liter samples five minutes before the end of each period, as is done at the Russell Sage Institute of Pathology [6] and by Murlin.[3]

The balance which weighs the oxygen cylinder and the absorbing bottles is accurate to 10 mg. The residual samples are weighed to 0.1 mg. The absorbing trains are tested for tightness before the beginning of each period. The entire apparatus is also tested at frequent intervals. Besides this, numerous alcohol checks are made throughout the experimental year.

The technic during observations is essentially that outlined by Lusk [6] for indirect calorimetry with a closed circuit apparatus. The mercurial thermometers are read immediately after the close of each period.

CALCULATION OF RESULTS

The heat production of the children is calculated from the carbon dioxid produced, the oxygen consumed, and the nitrogen excreted in the urine during calorimeter periods of two to three hours. The oxygen is multiplied by the caloric value of 1 liter of oxygen at the observed non-protein respiratory quotient. This value is obtained from the Zuntz-Schumberg table,[7] modified by Lusk.[8] The urine is collected preceding the start of the observation, and the calorimeter specimen at its termination. The time of both voidings is noted. When the nitrogen of the calorimeter specimen, which is used as a basis for determining the protein metabolism, was calculated in terms of twenty-four hours, it varied little from the total daily nitrogen excretion. A sample calculation may be found in the recent book of Du Bois.[9]

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6. Lusk, G.: Clinical Calorimetry. I. A Respiration Calorimeter for the Study of Disease, Arch. Int. Med. **15**:793 (May) 1915.

7. Zuntz, N., and Schumberg: Studien zu einer Physiologie des Märches, Berlin, 1901, p. 361.

8. Lusk, G.: Analysis of the Oxidation of Mixtures of Carbohydrate and Fat —a Correction, J. Biol. Chem. **59**:41 (Feb.) 1924.

9. Du Bois, E. F.: Basal Metabolism in Health and Disease, Philadelphia and New York, Lea & Febiger, 1924, p. 71

Only the average figures of two or more hourly periods are used in computing the results. However, in these observations the heat production for individual periods approximated the average figures. In one instance, the deviation reached 7 per cent., while in the remaining seven observations the fluctuations for individual periods were between 1 and 4 per cent. from the average results. Further evidence that the results represent the basal metabolism of the children is found in their close agreement with determinations made on other days. All figures are independently calculated by both observers.

ALCOHOL CHECKS

Following the custom of the Russell Sage Institute,[10] we are publishing all the alcohol checks for the experimental year in this first communication. The results appear in Table 1.

The average error for the oxygen consumption, on which the heat production is based, was minus 0.9 per cent. The maximum error on Nov. 19, 1924, was minus 2.6 per cent. If this maximum error be applied to the calculation of the average 800 calories produced in twenty-four hours by the children in this series, it would not exceed 21 calories. In most instances, the error is undoubtedly less than this. Furthermore, the alcohol burned was so regulated that the heat dissipated per hour closely approximated the heat produced by the children in this group.

PREPARATION OF SUBJECTS

All the children were in the metabolism ward for at least two weeks, and were trained in their part of metabolism technic. From three to eight calorimeter observations were made on each child, and, for several days preceding determinations, practice periods were repeatedly run. This paper includes only the determinations in which the children slept throughout the two or more hours, and which yielded the minimal results.

Children remained in bed on the morning of the observation. Three of the seven children received a light breakfast not exceeding 310 calories and 12.3 gm. of protein. From five to thirty-six hours elapsed between the last meal and the start of the experiment. After voiding, the child was weighed (weight of clothes deducted), and the standing height measured. The rectal temperature was then taken, and the patient was carried to the respiration chamber where the stethoscope was applied and the pneumograph adjusted. When the patient was comfortable, the cover was lowered. Two children excreted small quantities of acetone bodies in their urine, not exceeding 1 gm., on the day of observation.

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10. Riche, J. A., and Soderstrom, G. F.: Clinical Calorimetry. II. The Respiration Calorimeter of the Russell Sage Institute of Pathology in Bellevue Hospital, Arch. Int. Med. **15**:805 (May) 1915.

TABLE 1.—*Alcohol Checks for Experimental Year*

Date	Minutes	Alcohol, Gm.	Water			Carbon Dioxid			Oxygen			Respiratory Quotient (Theory 0.667)		Heat Theory, Calories
			Theory, Gm.	Found, Gm.	Error, per Cent.	Theory, Gm.	Found, Gm.	Error, per Cent.	Theory, Gm.	Found, Gm.	Error, per Cent.	Found	Error, per Cent.	
Nov. 5.....	60	6.44	8.20	8.16		12.30	12.43		13.42	13.41		0.674		
	60	6.70	8.54	8.62		12.80	12.74		13.96	13.92		0.666		
	60	6.40	8.16	8.17		12.23	12.19		13.34	13.40		0.662		
	Average	6.51	8.30	8.32	+0.2	12.44	12.45	+0.1	13.57	13.58	+0.1	0.667	±0.0	46.10
Nov. 7.....	60	5.92	7.54	7.99		11.31	11.42		12.34	11.73		0.708		
	60	5.85	7.45	7.55		11.17	11.08		12.19	11.82		0.682		
	60	6.07	7.73	7.80		11.60	11.41		12.65	12.75		0.651		
	30	2.96	3.77	3.79		5.66	5.77		6.17	6.63		0.633		
	Average	5.20	6.63	6.78	+2.4	9.93	9.92	−0.2	10.84	10.73	−1.0	0.672	+0.7	36.80
Nov. 10....	60	6.88	8.77	8.79		13.15	13.24		14.35	14.18		0.679		
	45	5.33	6.79	6.67		10.18	10.08		11.11	11.10		0.660		
	45	5.14	6.55	6.79		9.83	10.11		10.72	11.41		0.644		
	30	3.51	4.48	4.31		6.72	6.57		7.33	7.00		0.683		
	30	3.63	4.62	4.53		6.93	6.72		7.56	7.44		0.657		
	Average	4.90	6.24	6.22	−0.3	9.36	9.34	−0.2	10.21	10.23	+0.1	0.665	−0.3	34.68
Nov. 12....	30	....	....	4.01		.....	5.86		.....	6.35		0.671		
	30	....	....	3.83		.....	5.55		.....	5.78		0.698		
	30	....	....	4.04		.....	5.83		.....	6.46		0.656		
	30	....	....	3.75		.....	5.56		.....	5.84		0.692		
	Average	2.96	3.77	3.91	+3.7	5.66	5.70	+0.7	6.17	6.11	−1.0	0.679	+1.8	20.96
Nov. 19....	45	5.59	7.12	7.38		10.68	10.73		11.65	11.39		0.685		
	45	5.70	7.26	7.24		10.89	10.69		11.88	11.34		0.686		
	60	7.47	9.53	9.60		14.28	14.12		15.58	15.55		0.660		
	30	4.81	6.13	6.19		9.19	9.17		10.03	9.56		0.698		
	Average	5.89	7.51	7.60	+1.2	11.26	11.18	−0.7	12.28	11.96	−2.6	0.680	+1.9	41.70
Nov. 21....	30	2.92	3.73	3.81		5.59	5.55		6.09	5.99		0.674		
	30	2.81	3.58	3.63		5.37	5.44		5.86	5.80		0.682		
	30	2.77	3.54	3.64		5.30	5.31		5.78	5.84		0.661		
	30	2.74	3.49	3.54		5.23	5.19		5.71	5.60		0.674		
	30	2.74	3.49	3.54		5.23	5.20		5.71	5.68		0.666		
	30	2.59	3.30	3.41		4.95	5.08		5.40	5.56		0.665		
	Average	2.76	3.52	3.60	+2.3	5.27	5.30	+0.3	5.75	5.75	−0.2	0.670	+0.4	19.54
Nov. 24....	30	2.89	3.68	3.74		5.51	5.48		6.02	5.69		0.700		
	30	2.89	3.68	3.73		5.51	5.44		6.02	5.90		0.671		
	30	2.85	3.63	3.77		5.44	5.56		5.94	6.18		0.654		
	30	2.89	3.68	3.78		5.51	5.54		6.02	6.17		0.653		
	30	2.81	3.58	3.66		5.37	5.36		5.86	5.74		0.679		
	30	2.89	3.68	3.66		5.51	5.46		6.02	6.04		0.657		
	Average	2.87	3.65	3.72	+1.9	5.48	5.47	±0.0	5.98	5.95	−0.4	0.669	+0.3	20.30

Dec. 1.....	30	3.44	4.39	6.67		6.58	6.58		7.17	6.93		0.691		
	30	3.44	4.39	6.63		6.58	6.49		7.17	6.98		0.676		
	30	3.48	4.43	6.60		6.65	6.72		7.25	7.57		0.646		
	30	3.51	4.48	6.69		6.72	6.83		7.33	7.54		0.659		
	Average	3.47	4.42	6.65	+50.3*	6.63	6.66	+0.3	7.23	7.26	+0.3	0.667	±0.0	24.57
Jan. 1.....	60	5.69	7.25	7.14		10.87	10.83		11.86	11.79		0.668		
	60	5.73	7.29	7.16		10.96	10.85		11.94	11.75		0.672		
	Average	5.71	7.27	7.15	−1.7	10.91	10.84	−0.6	11.90	11.77	−1.1	0.670	+0.4	40.41
Feb. 4.....	60	5.99	7.63	8.04		11.44	11.48		12.48	12.05		0.693		
	60	5.95	7.58	8.18		11.37	11.33		12.40	12.22		0.674		
	Average	5.97	7.60	8.11	+6.6	11.40	11.41	±0.0	12.44	12.14	−2.5	0.684	+2.5	42.24
Feb. 11.....	60	4.30	5.48	7.47		8.21	8.25		8.96	9.31		0.644		
	60	3.82	4.86	6.49		7.29	7.38		7.96	7.52		0.714		
	Average	4.06	5.17	6.98	+35.0*	7.75	7.82	+0.8	8.46	8.42	−0.5	0.675	+1.2	28.72
Feb. 13.....	60	6.41	8.17	9.60		12.25	12.28		13.36	13.22		0.676		
	60	6.45	8.22	9.43		12.32	12.23		13.44	13.43		0.662		
	Average	6.43	8.19	9.52	+16.2*	12.28	12.26	−0.2	13.40	13.33	−0.6	0.669	+0.3	45.51
March 9....	60	6.67	8.50	8.65		12.74	12.73		13.90	13.86		0.668		
	60	6.41	8.17	8.32		12.25	12.20		13.36	12.97		0.684		
	Average	6.54	8.33	8.49	+1.8	12.50	12.47	−0.2	13.63	13.42	−1.6	0.676	+1.3	46.29
March 20...	60	6.11	7.79	8.36		11.68	11.79		12.74	12.93		0.663		
	60	6.08	7.74	8.42		11.61	11.49		12.67	12.11		0.690		
	Average	6.09	7.77	8.39	+8.0	11.65	11.64	±0.0	12.70	12.52	−1.5	0.676	+1.3	43.15
March 25...	60	6.37	8.12	8.68		12.18	12.27		13.28	13.30		0.671		
	60	6.37	8.12	8.71		12.18	12.08		13.28	13.75		0.639		
	60	6.45	8.22	8.59		12.32	12.25		13.44	12.22		0.729		
	Average	6.40	8.15	8.66	+6.3	12.22	12.20	−0.2	13.33	13.09	−1.8	0.678	+1.6	45.29
March 30...	60	5.56	7.08	7.62		10.62	10.70		11.58	12.02		0.647		
	60	5.56	7.08	6.99		10.62	10.39		11.58	11.07		0.688		
	60	5.45	6.94	7.13		10.41	10.51		11.35	11.82		0.647		
	60	5.48	6.99	6.89		10.48	10.20		11.43	11.27		0.658		
	Average	5.51	7.02	7.16	+2.0	10.53	10.45	−0.8	11.49	11.55	+0.5	0.658	−1.3	39.02
April 8.....	60	4.59	5.85	6.01		8.78	9.02		9.58	9.42		0.696		
	60	4.71	6.00	6.09		8.99	8.97		9.81	10.49		0.622		
	60	4.52	5.76	6.00		8.64	8.76		9.42	9.48		0.672		
	Average	4.61	5.87	6.03	+2.7	8.80	8.92	+1.4	9.60	9.80	+2.1	0.662	−0.7	32.61
May 1.....	60	5.48	6.99	7.42		10.48	10.56		11.43	11.53		0.666		
	60	5.56	7.08	7.06		10.62	10.22		11.58	11.08		0.671		
	Average	5.52	7.04	7.24	+2.9	10.55	10.39	−1.5	11.51	11.31	−1.7	0.668	+0.1	39.08
May 22.....	60	5.63	7.18	7.56		10.76	10.56		11.74	11.35		0.677		
	60	5.56	7.08	7.33		10.62	10.46		11.58	11.65		0.653		
	Average	5.60	7.13	7.45	+4.5	10.69	10.51	−1.7	11.66	11.50	−1.4	0.665	−0.3	39.61
Total average.....		105.80	108.83	+2.9	185.31	184.93	−0.2	202.15	200.42	−0.9	0.671	+0.6	

* Water replaced oil in seal (not included in averages).

The case histories will be reported in detail in subsequent communications. A brief summary follows:

CASE HISTORIES

CASE 1.—T. M., a girl, white, aged 6½ years, had been subject to generalized epileptic seizures, recurring frequently since 1923. She entered the metabolism ward on Dec. 8, 1924, at which time physical examination was negative. She was mentally precocious and cooperated well. During her stay of two weeks, she was free from attacks. Blood and spinal fluid, including the Wassermann reaction of both, were negative. A cutaneous tuberculin test was also negative. A diagnosis of idiopathic epilepsy was made.

CASE 2.—E. F., a girl, Jewish, born Sept. 11, 1914, was admitted to the metabolism ward Dec. 28, 1924, for observation. She had previously entered the hospital in July, 1924, complaining of poor appetite and stationary weight of one year's duration. At that time she was moderately underweight. After several foci of infection were removed, she remained well up to the time of her second admission. Laboratory examinations were all negative except for the intracutaneous tuberculin reaction with 0.2 mg. A roentgenogram of the chest showed some widening of the hilum shadow, suggesting an old, healed tubuerculous process of the mediastinal nodes.

CASE 3.—L. A., a girl, white, born Feb. 18, 1918, entered the hospital on Dec. 18, 1924, for recurrent attacks of infectious nephritis. During the month that she was on the metabolism service, she was afebrile and symptomless, and her urine was clear. Physical examination was essentially negative. Cutaneous and intracutaneous tuberculin tests were negative

CASE 4.—E. B., a boy, white, born June 4, 1918, was admitted to the metabolism ward for study. There were no complaints and the examination was negative. The state of nutrition was normal. The Wassermann and tuberculin reactions were negative. This patient was a normal, healthy child.

CASE 5.—N. H., a girl, white, born Aug. 20, 1918, entered the metabolism service April 7, 1925, for attacks of cyclic vomiting since 1920. Her last attack occurred during the week of March 9, 1925, at which time acetone bodies were present in the urine and breath. She was somewhat undernourished and her tonsils were diseased. The Wassermann and tuberculin reactions were negative. A more detailed account will appear in a subsequent communication.

CASE 6.—F. A., a boy, white, born Nov. 25, 1914, was admitted to the metabolism ward April 7, 1925, with diabetes mellitus, recognized first in February, 1925. He was markedly below normal weight. Physical examination, the Wassermann and tuberculin tests were negative.

CASE 7.—S. A., a girl, white, obese, born April 18, 1918, entered the hospital April 27, 1925, for observation. She had been consistently overweight for her age since she was 18 months old. The adipose tissue was symmetrically distributed over her body. Roentgenogram of the skull showed no abnormal findings. Tuberculin and Wassermann tests were negative. During the month of her stay, she was put on a restricted diet of 1,000 calories and she lost 7 pounds.

COMMENT

The details of the calorimeter observations appear in Table 2.

TABLE 2.—*Calorimeter Data in Terms of Averages Per Hour*

Experiment	Case	Date	Weight, Kg.	Height, Cm.	Surface Area, Sq. M.	Time of Observation	Carbon Dioxid, Gm.	Oxygen, Gm.	Respiratory Quotient	N_2 per Hour, Gm.	Calories, per Hour	Pulse, Average	Temperature Average, F.	Remarks
4	1	12/15/24	20.0	103.0	0.74	11:39 a. m. to 2:39 p. m.	11.0	9.7	0.83	0.187	32.4	89	98.6	Asleep; calories, 276; protein, 12.3 gm.; 5½ hours after eating
5	1	12/22/24	....	.....	.....	11:16 a. m. to 1:16 p. m.	11.0	10.0	0.80	0.181	33.4	95	98.8	Asleep; 13 hours after eating
51	5	5/13/25	19.8	115.0	0.795	4:30 p. m. to 6:30 p. m.	10.9	9.4	0.85	0.137	31.7	76	98.8	Asleep; calories, 242; protein, 5.9 gm.; 6¼ hours after eating
17	3	1/22/25	18.0	118.5	0.74	6:14 p. m. to 8:14 p. m.	9.8	9.5	0.75	0.219	31.0	73	98.3	Asleep; slight ketonuria; 36 hours after eating
55	7	5/18/25	41.5	126.0	1.165	11:50 a. m. to 2:20 p. m.	15.2	13.4	0.83	0.116	45.2	82	99.1	Asleep; calories, 310; protein, 5.8 gm.; 5½ hours after eating
12	2	1/14/25	22.4	127.0	0.90	10:10 a. m. to 12:10 p. m.	11.4	10.7	0.78	0.173	35.4	76	98.1	Asleep; slight ketonuria; 36 hours after eating
26	4	3/ 2/25	20.7	118.5	0.825	11:02 a. m. to 1:02 p. m.	11.5	10.7	0.78	0.291	35.3	58	97.4	Asleep 1 hour; quiet 1 hour; calories, 165; protein, 8.3 gm.; 5 hours after eating
48	6	5/ 8/25	26.2	137.0	1.015	10:45 a. m. to 12:45 p. m.	10.3	9.5	0.79	0.152	31.5	61	99.0	Asleep; 28¾ hours after eating

BASAL METABOLISM OF NORMAL CHILDREN

The weight of the four girls (Experiments 4, 51, 17 and 12) who were aged from 6½ to 10 years, and the one boy (Experiment 26) aged 7 years, varied from minus 19 to plus 18 per cent. from the average figures derived from the height-weight table for age of Baldwin and Wood.[11] Their minimal energy requirement ranged between 39.3 and 43.8 calories per square meter per hour; and between 38.0 and 41.4 calories per kilogram per twenty-four hours. The boy's heat production was slightly

TABLE 3.—*Summary of Basal Metabolism*

Experiment	Case	Weight, Kg.	Height, Cm.	Surface Area, Sq. M.*	Calories per 24 Hours	Calories per Sq. M. per Hour	Calories per Kg. per 24 Hours
4†	1	20.0	103.0	0.74	778	43.8	38.9
51	5	19.8	115.0	0.795	761	39.9	38.4
17	3	18.0	118.5	0.74	745	41.9	41.4
12	2	22.4	127.0	0.90	848	39.3	38.0
26	4	20.7	118.5	0.825	848	42.8	41.0
55	7	41.5	126.0	1.165	1,085	38.8	26.1
48	6	26.2	137.0	1.015	757	31.1	28.9
5‡	1	20.0	103.0	0.74	801	45.1	40.1

* The surface area column was obtained from the Boothby and Sandiford diagram of the Du Bois height-weight formula.
† This experiment was made five and one half hours after a meal.
‡ This experiment was made in the postabsorptive state.

TABLE 4.—*Comparison of the Basal Metabolism with the Standards of Benedict*

Experiment	Case	Percentage Variation from Average Weight*	Percentage Variation from Average Height*	Percentage Variation from Average Calories per Kg. per 24 Hours†	Percentage Variation from Average Total Calories Ref. to Body Weight†	Percentage Variation from Average Total Calories Ref. to Standing Height‡	Percentage Variation from Average Calories per Sq. M. per Hour†
4	1	+18	— 9	— 3	— 8	+11	+ 6
51	5	— 4	+ 2	— 4	— 5	— 7	— 3
17	3	—19	+10	+ 5	— 2	—13	+ 2
12	2	—16	+ 7	+ 3	— 3	— 9	— 2
26	4	— 8	+ 4	+ 3	— 3	....	— 4
55	7	+65	§	—34	§	+17	— 6
48	6	—18	+ 8	—20	—26	....	—24

* Average figures obtained from tables of Baldwin and Wood.
† Average figures obtained from table and smoothed curves of Benedict and Talbot.
‡ Average figures from table of Benedict.
§ Standard table does not include figure for this weight.

higher than that of the three girls of the same age. The 10 year old girl had a lower basal metabolism than the three girls aged from 6 to 10 years (Table 3). The basal metabolism for these five children was within 6 per cent. of the various standards proposed by Benedict and Talbot.[1] It did not matter whether the standards used were based on body surface or on body weight. When based on standing height the variation was greater, being minus 13 to plus 11 per cent. for the four girls [12] (Table 4).

11. Baldwin, B. T., and Wood, T. D.: Height-Weight Table for Different Ages, American Child Health Association, 1924.

12. Benedict, F. G.: Physical Factors in Predicting the Basal Metabolism in Girls, Proc. Am. Philosoph. Soc. **63**:25 (April) 1924.

These results suggest that there is little choice in the selection of a standard for predicting the basal metabolism of children of normal stature. This is in accord with the conclusions of other observers working with adults,[13] new-born infants [14] and older infants.[15]

BASAL METABOLISM IN OBESITY

In the one girl (Experiment 55), aged 7 years, who was 65 per cent. overweight,[11] the heat production varied minus 34 and plus 17 per cent. from the average figures when referred to body weight [1] and standing height [12] respectively. When referred to body surface the variation was only minus 5 per cent. (Table 4).

As pointed out by Boothby [13] and Krogh,[13] and in contrast to Means and Woodwell,[13] the surface area in this obese girl was a better criterion than other standards for predicting the basal metabolism. The first two authors came to the same conclusion in work on adults of unusual proportions. Talbot found a low metabolism by all standards in an obese child with a small sella turcica.[16]

BASAL METABOLISM IN THE MALNUTRITION OF DIABETES

In the boy, aged 11 years, with diabetes (Experiment 48), the basal metabolism varied proportionately with the degree of malnutrition. He was 18 per cent. below the average weight and his basal requirement was 20 to 26 per cent. below all of the standards (Table 4). This is in agreement with the results of Richardson and Mason,[17] and Wilder, Boothby and Beeler,[18] who found the same to be true in the malnutrition of diabetic adults.

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13. Means, J. H., and Woodwell, M. N.: Remarks of Standards for Normal Basal Metabolism, Arch. Int. Med. **27**:608 (May) 1921. Krogh, A.: Determination of Standard Metabolism of Patients by a Recording Apparatus, Boston M. & S. J. **189**:313 (Aug. 30) 1923. Boothby, W. M., and Sandiford, I.: A Comparison of the Du Bois and the Harris and Benedict Normal Standards for the Estimation of the Basal Metabolic Rate, J. Biol. Chem. **54**:767 (Dec.) 1922.

14. Murlin, J. R.: Abt's Pediatrics, Philadelphia, W. B. Saunders Company, **1**:601, 1923.

15. Murlin, J. R., and Hoobler, B. R., The Energy Metabolism of Ten Hospital Children Between the Ages of Two Months and One Year, Am. J. Dis. Child. **9**:81 (Feb.) 1915.

16. Talbot, F. B.: Studies in Metabolism; II. Metabolism of a Very Obese Child with a Small Sella Turcica (Typus Frölich), Am. J. Dis. Child. **20**:331 (Oct.) 1920.

17. Richardson, H. B., and Mason, E. H.: Clinical Calorimetry 33; the Effect of Fasting in Diabetes as Compared with a Diet Designed to Replace the Food-Stuffs Oxidized During a Fast, J. Biol. Chem. **57**:587 (Sept.) 1923.

18. Wilder, R. M.; Boothby, W. M., and Beeler, C.: Studies of the Metabolism of Diabetes, J. Biol. Chem. **51**:311 (April) 1922.

EFFECT OF A LIGHT MEAL ON THE BASAL METABOLISM

In Experiments 4 and 5 (Table 2), the heat production of the same child was compared five and one-half hours and thirteen hours following a meal containing 276 calories and 12.3 gm. of protein. So far as we could determine, all the other conditions were identical. The metabolism was slightly lower after the meal (32.4 calories per hour) than in the postabsorptive state (33.4 calories per hour).

This confirms the results of Bauer and Blunt [19] working with children, and Benedict and Benedict [20] and Soderstrom, Barr and Du Bois [21] working with adults, that there is no appreciable increase in the heat production four to six hours after a light meal. In view of this, we considered the heat production of the three other children who were studied five to six hours following a meal to be strictly basal, since in these observations the meals were all smaller than in Experiment 5.

SUMMARY AND CONCLUSIONS

1. The apparatus and technic for measuring the respiratory exchange of children have been described.

2. The minimal energy requirement in five normal children was found to be within plus or minus 6 per cent. of the standards established by Benedict and Talbot.

3. The body surface and body weight were equally good standards for predicting the basal metabolism in these five children of normal stature.

4. In one overweight girl, the body surface was found to be a better criterion for prediction than the body weight.

5. In one diabetic boy, the lowering of the basal requirement was proportional to the degree of malnutrition.

6. The basal metabolism in one girl was not increased five hours after a light meal.

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19. Bauer, V., and Blunt, K.: Effect of a Small Breakfast on the Energy Metabolism of Children, J. Biol. Chem. **59**:77 (Feb.) 1924.

20. Benedict, F. G., and Benedict, C. G.: A Permissible Breakfast Prior to Basal Metabolism Measurements, Boston M. & S. J. **188**:849 (May 31) 1923.

21. Soderstrom, G. F.; Barr, D. P., and Du Bois, E. F.: Clinical Calorimetry. 26. The Effect of a Small Breakfast on the Heat Production, Arch. Int. Med. **21**:613 (May) 1918.

THE RESPIRATORY METABOLISM IN INFANCY AND IN CHILDHOOD

II. KETOSIS AND THE RESPIRATORY EXCHANGE IN CHILDREN *

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NEW YORK

INTRODUCTION

Ketosis is a common event during childhood. Acetone bodies usually appear in the urine and breath of children following operative procedures; they frequently accompany acute infections, and their presence may readily be induced by fasting and by low carbohydrate, high fat diets. This tendency is accentuated in a specific group of children, some of whom develop so-called "cyclic vomiting."

Measurements of the respiratory exchange of children in ketosis are not available in the literature. We are, therefore, presenting data on six children which correlate the ketogenic balance of the metabolized foodstuffs, as determined in the respiration chamber, with the excretion of ketone bodies in the urine. Various degrees of ketosis were induced by fasting and by diets containing progressively increasing proportions of fat to carbohydrate. The dietary group of experiments was also made use of to compare the foodstuffs ingested with the foodstuffs metabolized.

The investigation is concerned specifically with the following questions: 1. Do children oxidize foodstuffs in the proportions contained in their diets? 2. Is the relation of the oxidized to the ingested foodstuffs the same in children subject to cyclic vomiting as in normal children? 3. Is the adult relation of the metabolic ketogenic balance to the excretion of ketone bodies maintained in children?

REVIEW OF THE LITERATURE

The extensive researches of Shaffer [1] and Woodyatt [2] establish the theory that ketogenesis depends on the ketogenic balance of the food-

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1. Shaffer, P. A.: Antiketogenesis. I. An In Vitro Analogy, J. Biol. Chem. **47**:433 (July) 1921; Antiketogenesis. II. The Ketogenic Antiketogenic Balance in Man, ibid, **47**:449 (July) 1921; Antiketogenesis. III. Calculation of the Ketogenic Balance from the Respiratory Quotients, ibid. **49**:143 (Nov.) 1921; Antiketogenesis. IV. The Ketogenic-Antiketogenic Balance in Man and Its Significance in Diabetes, ibid, **54**:399 (Oct.) 1922; Antiketogenesis. V. The Ketolytic Reaction; Action of Glycol Aldehyde and of Glyoxal, ibid, **61**:585 (Oct.) 1924. Antiketogenesis: Its Mechanism and Significance, The Harvey Society Lectures, Philadelphia, J. B. Lippincott Company, pp. 105-136, 1923-1924.

2. Woodyatt, R. T.: Objects and Method of Diet Adjustment in Diabetes, Arch. Int. Med. **28**:125 (Aug.) 1921.

stuffs undergoing oxidation in the body. Shaffer assigned theoretic ketogenic and antiketogenic values to the various foodstuffs, and calculated from the available respiratory data their ratio in the metabolic mixture when keto-acids first appeared in abnormal amounts in the urine. He found the molecular ratio to be approximately 1.0 at the threshold of ketosis. Woodyatt had previously proposed a similar ratio on the basis of clinical experience. Shaffer subsequently succeeded in obtaining better agreement between the expected and actually excreted ketone bodies in cases of marked ketosis by doubling the value originally ascribed to the antiketogenic material, thereby making the ratio 2.0. Woodyatt expresses the ratio in terms of grams of fatty acids to glucose (F.A.:G.), Shaffer expresses it as gram molecules of ketogenic (fatty acids) to antiketogenic (total glucose) material (K.:A.). The approximate K.: A. ratio may be obtained at any level of ketosis by dividing the F.A.: G. ratio by 1.5. Richardson and Ladd [3] have recently confirmed Shaffer's and Woodyatt's conclusions at the borderline of ketogenesis. They found that the metabolic fatty acid glucose ratios, as determined by the calorimeter, were between 1.2 and 1.7 (equivalent to K.: A. ratios of approximately 0.8 to 1.1), before the urinary excretion of ketone bodies became significant. Wilder and Winter,[4] Ladd and Palmer,[5] and Wilder, Boothby and Beeler [6] found higher K.: A. ratios at the ketogenic threshold, approaching 2.0. Other investigations on antiketogenesis are fully reviewed in Shaffer's [1] articles. Stated briefly, all workers have shown that the excretion of ketone bodies in the urine is very slight, so long as the metabolic ketogenic-antiketogenic and the fatty acid glucose ratios are maintained below 1.0 and 1.5 respectively.

The literature showing the relation of the ketogenic balance to ketogenesis has been almost entirely limited to data derived from studies of adults. No similar investigations, to our knowledge, have been made in children, although clinical observers agree that children are particularly subject to ketosis. Allen [7] compared the ketosis of normal mature dogs and of puppies during fasting and while on high fat diets. Under similar experimental conditions, the adult animals developed only a trivial ketosis, while in the puppies the reaction was severe. The author believes this difference to be the result of a special biologic factor in ketosis not entirely explained by the relative proportions of fatty acids

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3. Richardson, H. B., and Ladd, W. S.: Clinical Calorimetry. 34. Ketosis and Respiratory Exchange in Diabetes, J. Biol. Chem. **58**:931 (Jan.) 1924.

4. Wilder, R. M., and Winter, M. D.: The Threshold of Ketogenesis, J. Biol. Chem. **52**:393 (June) 1922.

5. Ladd, W. S., and Palmer, W. W.: The Use of Fat in Diabetes Mellitus and the Carbohydrate-Fat Ratio, Am. J. M. Sc. **166**:157 (Aug.) 1923.

6. Wilder, R. M.; Boothby, W. M., and Beeler, C.: Studies of the Metabolism of Diabetes, J. Biol. Chem. **51**:311 (Jan.) 1922.

7. Allen, F. M.: Experimental Studies in Diabetes, Series V; Acidosis (3), Acidosis in Dogs Without Glycosuria (4), Acidosis in Puppies (5), Acidosis in Phlorizinized Dogs, J. Metabol. Res. **1**:189, 199, 223, 1923.

and glucose metabolized. During short periods of fasting, the association of ketosis with hypoglycemia has been noted in infants by Rumpf,[8] and in children by Shaw and Moriarty,[9] and other workers.[10] Ross and Josephs[11] obtained minimum blood sugar values during fasting in a child subject to cyclic vomiting sooner than in three normal children. The ketonuria, however, was more marked in the normal children, both during fasting and while on high fat diets.

METHODS

A detailed description of the metabolism ward and of the methods follows, in order to avoid repetition in subsequent communications of this series.

The metabolism unit is organized on the plan of the Russell Sage Institute of Pathology.[12] The patients under observation occupy the beds in the ward nearest the calorimeter room. Two special nurses and one nursery maid, all of whom are thoroughly trained in metabolism technic, are assigned solely to the care of these patients. They are always within sight of one of these nurses during both day and night. At no time are more than three children investigated simultaneously. Throughout these experiments the children were contented and cooperative.

Diets.—Diets are prepared in a special diet kitchen on the same floor as the calorimeter room. Foods are weighed accurately to 0.1 Gm. Care is taken to please each child, and throughout these investigations all food offered was quantitatively eaten. Foods are of the simplest kinds, and whenever possible are eaten from the dishes in which they are prepared. The composition of the diets is calculated from the tables of Mary Swartz Rose.[13] The fluid intake, exclusive of the water content of the ingested solid foods, was kept constant throughout the periods of observation, and was between 2,000 and 2,400 cc. daily for each child. Diets for each day were apportioned into six equal parts and were given at four hour intervals.

8. Rumpf, F.: Uber den Blutzucker in Hunger und uber die glykamische Reaktion nach kleinen Dosen Zucker beim Saugling und Kleinkinde, Jahrb. f. Kinderh. **105**:321, 1924.

9. Shaw, E. B., and Moriarty, M.: Hypoglycemia and Acidosis in Fasting Children with Idiopathic Epilepsy, Am. J. Dis. Child. **28**:553 (Nov.) 1924.

10. Hoeffel, G., and Moriarty, M.: The Effects of Fasting on the Metabolism of Epileptic Children, Am. J. Dis. Child. **28**:16 (July) 1924. Talbot, F. B.; Shaw, E. B., and Moriarty, M.: Hypoglycemia and Acidosis, J. A. M. A. **83**:91 (July 12) 1924.

11. Ross, S. G., and Josephs, H. W.: Observations on the Metabolism of Recurrent Vomiting, Am. J. Dis. Child. **28**:447 (Oct.) 1924.

12. Gephart, F. C., and Du Bois, E. F.: The Organization of a Small Metabolism Ward, Arch. Int. Med. **15**:829 (May) 1915.

13. Rose, Mary Swartz: Laboratory Handbook of Dietetics, Ed. 2, New York, The Macmillan Company, 1923.

Urine.—Urine specimens are collected separately, as is done at the Russell Sage Institute of Pathology.[12] Directly after voiding, each specimen is preserved with chloroform and thymol. Every morning, the single specimens are carried to the laboratory, in which they are combined for twenty-four hour determinations or are analyzed separately. Nitrogen is determined by the Kjeldahl method. The total acetone bodies are determined by the method of Van Slyke[14] and expressed as acetone. Total organic acids are determined by the method of Van Slyke and Palmer,[15] corrected for the actually determined creatinin content, and expressed as cubic centimeters of tenth normal acid in total specimens. Calorimeter specimens are obtained as described in the previous paper,[16] and are used in the calculation of results. The individual constituents of the calorimeter urine (total nitrogen, acetone bodies and organic acids), when calculated for twenty-four hours, did not vary appreciably from the daily output, determined directly in the combined twenty-four hour specimen. In this investigation, qualitative analyses by Benedict's method demonstrated the absence of glucose in all specimens.

Blood.—Blood was withdrawn under oil before or after each calorimeter observation and was analyzed immediately for sugar by the Folin-Wu method,[17] for the carbon dioxid content by the method of Van Slyke and Stadie[18] and occasionally for total acetone bodies by the Van Slyke-Fitz method.[19]

Breath.—Acetone in the breath was determined qualitatively by use of the Scott-Wilson reagent,[20] and was found to be present whenever the urine contained acetone.

Feces.—No determinations of nitrogen or fat lost in the feces were made, but as none of the children had more than one well-formed stool daily during periods of study, we feel that the error entailed by not

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14. Van Slyke, D. D.: Studies of Acidosis. VII. The Determination of Beta-Hydroxibutyric Acid, Aceto-Acetic Acid and Acetone in Urine, J. Biol. Chem. **32**:455, 1917.

15. Van Slyke, D. D., and Palmer, W. W.: Studies of Acidosis. XVI. Titration of Organic Acid in Urine, J. Biol. Chem. **41**:567 (April) 1920.

16. Levine, S. Z., and Wilson, J. R.: The Respiratory Metabolism in Infancy and in Childhood. I. Basal Metabolism of Children, this issue, p. 323.

17. Folin, O., and Wu, H.: A System of Blood Analysis. Supplement I. A Simplified and Improved Method for Determination of Sugar, J. Biol. Chem. **41**: 367 (March) 1920. Rothberg, V. E., and Evans, F. A.: A Modified Folin and Wu Blood Sugar Method, J. Biol. Chem. **58**:443 (Dec.) 1923.

18. Van Slyke, D. D., and Stadie, W. C.: The Determination of the Gases of the Blood, J. Biol. Chem. **49**:1 (Nov.) 1921.

19. Van Slyke, D. D., and Fitz, R.: Studies of Acidosis. VIII. The Determination of Beta-Hydroxybutyric Acid, Aceto-acetic Acid, and Acetone in Blood, J. Biol. Chem. **32**:495, 1917.

20. Higgins, H. L.: The Determination of Acetone in the Breath, Bull. Johns Hopkins Hosp. **31**:447 (Dec.) 1920.

correcting for this loss is very slight. This assumption is confirmed by the results obtained by Weymuller,[21] who found no absolute increase in the fecal fat content even when the fat content of the diet was markedly raised.

EXPERIMENTAL PROCEDURE

Throughout experimental periods, the children were confined to bed and their activity was restricted. They were weighed at the same time each morning.

In the dietary experiments, the caloric intake of each child was made adequate to cover the maintenance requirement, which was estimated to exceed the basal metabolism by approximately 15 per cent. The latter was measured directly in one or more calorimeter observations. The protein content of diets was made adequate to cover the quantity metabolized as determined from the nitrogen excreted in the urine. That the caloric and protein values of the diets, as estimated, closely approximated the maintenance requirements of the children studied, is shown by the fact that their weights remained practically stationary, and that they were in approximate nitrogen equilibrium for the three or more weeks during which they received these diets. The initial diets of all the children contained low fatty acid glucose ratios, 0.4 to 0.5. The ratios were gradually and progressively raised at intervals of three to five days to 2.0 or 2.5 by increasing the fat at the expense of carbohydrate, without changing the total calories appreciably. In E. F. (Case 2) only, was the dietary ratio raised from 0.4 on January 27 directly to 2.0 on January 28.

One or more calorimeter observations were made after the children had been on each diet for three days, or longer. These periods were sufficiently long to avoid residual effects of previous diets. The observations were always begun four to six hours after the last meal.

In the starvation experiments, fasting was prolonged to the point of abnormal excretion of ketone bodies in the urine. During this time, the children received only small, noncaloric meals containing thrice-cooked 5 per cent vegetables, agar-agar jelly and fat-free broth. Analyses of these substances from time to time demonstrated the absence of starch and sugar.

From four to seven calorimeter observations were made on each child at approximately equivalent hours during the progress of the fast. They were never begun sooner than five hours after the last noncaloric meal.

RESPIRATORY METABOLISM

The technic and the results of alcohol checks for the entire year are fully described in the first paper of this series.[16] The results are based

21. Studies to be reported shortly from this laboratory.

TABLE 1.—*Calorimeter Data in Terms of Averages Per Hour*

Date	Weight, Kg.	Height, Cm.	Surface Area, Sq. M.	Time of Observation	Carbon Dioxide, Gm.	Oxygen, Gm.	Respiratory Quotient*	Nitrogen in Urine per Hour, Gm.	Calories	Temperature, Pulse Average	Temperature, Rectal, Aver.	Remarks †
Case 2:												
1/ 2/25	23.0	126.5	0.91	11:54 a. m. to 1:54 p. m.	14.28	12.76	0.82 0.81 0.81	0.162	42.7	95	100	Protein 41.9, fat 71.2, carbohydrate 212.2, calories 1,704, per 24 hours; on diet for four days. Fasting for 18 hours. Quiet
1/ 3/25	22.6	126.5	0.90	11:15 a. m. to 2:15 p. m.	14.72	13.71	0.77 0.81 0.76 0.78	0.262	45.4	109	98.8	Fast continued for 42 hours. Restless during third hour
1/13/25	22.7	127.0	0.90	3:05 p. m. to 6:05 p. m.	14.64	12.17	0.88 0.85 0.89 0.87	0.166	41.4	80	99.3	Protein 54, fat 78, carbohydrate 234, calories 1,906, per 24 hours. Last meal at 10 a. m. On diet for 5 days. Active during third hour
1/14/25	22.5	127.0	0.90	12:00 m. to 2:00 p. m.	13.42	11.89	0.85 0.80 0.82	0.147	39.9	83	99.3	Fast continued for 27 hours. Quiet
1/14/25	22.4	127.0	0.90	10:10 p. m. to 12:10 a. m.	11.41	10.68	0.77 0.79 0.78	0.173	35.4	76	98.1	Fast continued for 37 hours. Sleeping
1/15/25	21.8	127.0	0.89	2:05 p. m. to 4:05 p m.	12.86	12.08	0.75 0.79 0.78	0.200	39.9	91	99.5	Fast continued for 53 hours. Quiet
1/16/25	21.4	127.0	0.885	12:10 p. m. to 3:10 p. m.	12.09	11.82	0.76 0.77 0.72 0.74	0.247	38.7	101	99.2	Fast continued for 75½ hours. Quiet
1/27/25	22.8	127.0	0.90	3:25 p. m. to 6:25 p. m.	13.55	11.56	0.87 0.86 0.84 0.85	0.196	39.0	79	98.9	On same diet as of Jan. 13, 1925, for 11 days. Last meal at 10 a. m. Active during third hour
1/28/25	22.3	127.0	0.90	3:43 p. m. to 5:43 p. m.	13.34	11.53	0.87 0.82 0.84	0.209	38.8	81	99.1	Protein 45.7, fat 94.1, carbohydrate 16.7, calories 1,131, per 24 hours. On diet since 6:45 p. m. (Jan. 27, 1925). Last meal at 10 a. m. Active during second hour
1/29/25	22.0	127.0	0.895	3:15 p. m. to 5:15 p. m.	13.04	11.84	0.80 0.80 0.80	0.288	39.3	80	99.4	Diet of Jan. 28, 1925, continued for 44½ hours. Last meal at 10 a. m. Quiet
1/30/25	22.0	127.0	0.895	11:40 a. m. to 2:40 p. m.	13.55	12.63	0.79 0.81 0.75 0.78	0.325	41.6	85	99.2	Diet of Jan. 28, 1925, continued for 66½ hours. Last meal at 6:30 a. m. Active during third hour

Case 3:												
1/21/25	17.8	110.5	0.74	11:23 a. m. to 2:23 p. m.	14.20	11.35	0.91 0.95 0.88 0.91	0.130	39.0	110	100.1	Protein 34.4, fat 50.5, carbohydrate 180.2, calories 1,350, per 24 hours. On diet for 11 days. Last meal at 6:10 a. m. Active during second and third hours
1/22/25	17.6	110.5	0.735	8:28 a. m. to 9:58 a. m. and 11:05 a. m. to 12:05 p. m.	12.54	11.80	0.78 0.76 0.78	0 167	39.1	103	99.4	New preliminary period after I during which oxygen cylinder refilled. Fast continued for 28 hours. Quiet
1/22/25	18.0	110.5	0.74	6:14 p. m. to 8:14 p. m.	9.78	9.48	0.74 0.76 0.75	0.219	31.0	73	98.3	Fast continued for 37 hours. Sleeping
1/23/25	17.4	111.0	0.735	11:10 a. m. to 3:10 p. m.	11.98	11.19	0.77 0.76 0.80 0.79 0.78	0.209	37.0	99	99.5	Fast continued for 55 hours. Active during third period
Case 4:												
2/18/25	20.6	118.5	0.825	11:47 a. m. to 1:47 p. m.	14.68	12.72	0.84 0.84 0.84	0.191	42.8	63	98.9	Protein 25.0, fat 52.1, carbohydrate 100.1, calories 998, per 24 hours. Last meal at 10 a. m. On diet for 3 days. Active
2/20/25	20.5	118.5	0.825	10:48 a. m. to 12:48 p. m.	13.06	11.11	0.85 0.87 0.86	0.186	37.5	57	98.2	Same diet continued for 5 days. Last meal at 6 a. m. Active during second period
2/25/25	20.3	118.5	0.825	11:00 a. m. to 1:00 p. m.	12.64	11.03	0.87 0.80 0.83	0.303	36.8	56	97.7	Protein 50, fat 70.2, carbohydrate 8.7, calories 939, per 24 hours. On diet for 5 days. Last meal at 6 a. m. Quiet
3/ 2/25	20.7	118.5	0.825	11:02 a. m. to 1:02 p. m.	11.49	10.74	0.78 0.77 0.78	0.291	35.3	58	97.4	Protein 50, fat 80, carbohydrate 10, calories 990, per 24 hours. On diet for 5 days. Last meal at 6 a. m. Quiet
3/ 4/25	20.6	118.5	0.825	11:10 a. m. to 1:10 p. m.	12.87	11.70	0.78 0.82 0.80	0.324	38.7	65	97.7	Protein 50, fat 85, carbohydrate 2, calories 1,004, per 24 hours. On diet for 2 days. Last meal at 6 a. m. Active during second hour
3/ 5/25	20.4	118.5	0.825	3:15 p. m. to 5:15 p. m.	12.73	11.73	0.79 0.79 0.79	0.336	38.7	63	97.9	Diet continued for 3 days. Last meal at 10 a. m. Active during second hour
3/ 6/25	20.6	118.5	0.825	11:06 a. m. to 1:06 p. m.	13.33	12.27	0.80 0.78 0.79	0.338	40.5	60	98.4	Diet continued for 4 days. Last meal at 6 a. m. Active
3/ 7/25	20.7	118.5	0.825	2:56 p. m. to 4:56 p. m.	14.01	13.22	0.78 0.76 0.77	0.336	43.5	66	98.1	Protein 50, fat 86, carbohydrate 0.3, calories 1,006, per 24 hours. On diet for 1 day. Last meal at 10 a. m. Active

* The upper figures in this column give the respiratory quotients for individual periods.
† Daily diets were divided into six equal portions and given at four hour intervals.

TABLE 1.—*Calorimeter Data in Terms of Averages Per Hour—Continued*

Date	Weight, Kg.	Height, Gm.	Surface Area, Sq. M.	Time of Observation	Carbon Dioxide, Gm.	Oxygen, Gm.	Respiratory Quotient*	Nitrogen in Urine per Hour, Gm.	Calories	Temperature, Pulse Aver-	Temperature, Rectal, Aver.	Remarks †
Case 5:												
4/15/25	19.6	114.5	0.79	10:35 a. m. to 12:35 p. m.	14.04	12.03	0.86 0.84 0.85	0.164	40.6	99	98.6	Protein 35, fat 42, carbohydrate 90, calories 903, per 24 hours. On diet for 5 days. Last meal at 6:30 a. m. Moderately active
4/21/25	19.3	114.5	0.785	10:33 a. m. to 12:33 p. m.	13.38	12.56	0.75 0.80 0.78	0.173	41.6	..	99.4	Protein 40, fat 60, carbohydrate 44, calories 902, per 24 hours. On diet for 6 days. Last meal at 6:30 a. m. Active
4/24/25	19.3	114.5	0.785	10:49 a. m. to 12:50 p. m.	11.53	10.82	0.77 0.78 0.78	0.204	35.6	102	99.5	Protein 45, fat 72, carbohydrate 24, calories 953, per 24 hours. On diet for 3 days. Last meal at 6:15 a. m. Sleeping
4/25/25	19.1	114.5	0.78	10:45 a. m. to 12:45 p. m.	13.39	12.64	0.76 0.79 0.77	0.218	41.7	104	99.4	Same diet continued for 4 days. Last meal at 6:30 a. m. Active
4/29/25	19.1	114.5	0.78	10:52 a. m. to 12:55 p. m.	14.12	13.51	0.77 0.76 0.76	0.247	44.5	115	100.1	Protein 50, fat 76, carbohydrate 10, calories 953, per 24 hours. On diet for 4 days. Last meal at 6:30 a. m. Active during second hour
5/13/25	19.8	115.0	0.795	4:30 p. m. to 6:30 p. m.	10.92	9.40	0.83 0.86 0.85	0.137	31.7	76	98.8	Protein 35, fat 63, carbohydrate 175, calories 1,448, per 24 hours. On diet for 8 days. Last meal at 10:15 a. m. Sleeping. Moved several times
5/14/25	19.3	115.0	0.79	12:36 p. m. to 2:47 p. m.	12.47	10.91	0.82 0.84 0.83	0.215	36.6	84	98.6	Fast continued for 27½ hours. Active during second hour
5/15/25	18.9	115.0	0.78	11:55 a. m. to 2:01 p. m.	11.25	10.74	0.75 0.77 4.76	0.162	35.4	80	98.8	Fast continued for 50¾ hours. Active during second period
5/16/25	18.7	115.0	0.775	11:26 a. m. to 1:26 p. m.	11.87	11.30	0.78 0.75 0.76	0.207	37.2	94	99.0	Fast continued for 74¼ hours. Active

Case 6:												
4/14/25	27.6	137.5	1.035	10:18 a. m. to 1:18 p. m.	12.22	11.17	0.81 0.77 0.82 0.80	0.232	37.0	60	98.7	Protein 40, fat 78, carbohydrate 50, calories 1,094, per 24 hours. Last meal at 6.15 a. m. Quiet
4/17/25	27.3	137.0	1.030	10:28 a. m. to 12:28 p. m.	12.48	11.52	0.77 0.80 0.79	0.248	38.1	57	98.0	Protein 40, fat 60, carbohydrate 60, calories 968, per 24 hours. Last meal at 6:30 a. m. Moderately active second hour
4/22/25	26.8	137.0	1.025	11:03 a. m. to 1:03 p. m.	12.07	11.24	0.82 0.75 0.78	0.315	37.0	54	98.3	Protein 47, fat 74, carbohydrate 22, calories 971, per 24 hours. Last meal at 6:30 a. m. Active second hour
4/27/25	27.4	137.0	1.030	11:00 a. m. to 1:00 p. m.	12.68	11.76	0.80 0.78 0.79	0.180	38.9	60	98.6	Protein 50, fat 78, carbohydrate 10, calories 972, per 24 hours. Last meal at 6:30 a. m.. Moderately active
4/30/25	26.6	137.0	1.020	12:10 p. m. to 2:10 p. m.	13.14	12.06	0.78 0.80 0.79	0.275	39.9	58	98.7	Protein 52, fat 82, carbohydrate 0, calories 972, per 24 hours. Last meal at 6:30 a. m. Moderately active
5/ 8/25	26.9	137.0	1.02	11:34 a. m. to 2:34 p. m.	12.9	11.6	0.81 0.80 0.80 0.81	0.180	38.7	60	98.7	Last meal at 6:30 a. m. Active during third hour
5/ 9/25	26.2	137.0	1.015	10:45 a. m. to 12:45 p. m.	10.3	9.5	0.79 0.79 0.79	0.152	31.5	61	99.0	Fast continued for 29 hours. Slept throughout
5/10/25	26.4	137.0	1.015	10:26 a. m. to 12:26 p. m.	11.7	10.6	0.80 0.81 0.80	0.231	35.2	61	98.8	Fast continued for 53 hours. Quiet
5/11/25	26.1	137.0	1.015	11:05 a. m. to 2:05 p. m.	11.6	11.2	0.77 0.77 0.74 0.76	0.167	36.7	64	99.0	Fast continued for 78 hours. Active during third hour
Case 7:												
5/18/25	41.5	126.0	1.165	11:50 a. m. to 2:20 p. m.	15.2	13.4	0.83 0.80 0.83 0.84 0.83	0.116	45.2	82	99.1	Last meal at 6:20 a. m. Slept throughout
5/19/25	41.1	126.0	1.16	12:15 p. m. to 2:15 p. m.	17.9	16.2	0.80 0.81 0.80	0.145	54.2	88	99.6	Fast continued for 31 hours. Moderately active
5/20/25	40.6	126.0	1.16	11:00 a. m. to 1:00 p. m.	19.0	17.8	0.77 0.78 0.77	0.190	59.2	98	99.2	Fast continued for 54 hours. Active
5/21/25	39.7	126.0	1.16	12:45 p. m. to 2:45 p. m.	18.4	17.6	0.75 0.77 0.76	0.213	58.1	100	99.9	Fast continued for 79½ hours. Active

on forty-five calorimeter observations of two to four hours' duration. The children slept during the first one or two hours of most observations. They were then awakened and during the initial forty minutes of the last one or two hours, they duplicated closely their activity for the remaining part of the day during which they were awake. For the last twenty minutes of each active period the subjects remained absolutely quiet or fell asleep, in order to permit the respiration chamber to become stabilized before terminating the period. When the heat production was calculated from the calorimeter data in terms of twenty-four hours, it represented presumably the actual daily maintenance requirement both during fasting and while on the various diets. In the latter group of experiments, the daily difference between the heat production, as before calculated, and the caloric values of the maintenance diets was always less than 150 calories.

Alcohol Checks.—Respiratory quotients, which are used to calculate the foodstuffs oxidized, averaged 0.671 for all the alcohol checks, with maximum variations of 0.66 to 0.68 for individual determinations of two to three hours' duration, as against the theoretic quotient for alcohol of 0.667.[16] The consistently good agreement establishes the technical accuracy of the method.

Calculation of Results.—The total metabolism and the quantities of protein, fat, and carbohydrate oxidized were determined from the carbon dioxide produced, the oxygen consumed, and the nitrogen excreted in the urine during calorimeter periods of two to four hours. Computation by the customary method of indirect calorimetry, as employed by Lusk [22] was followed. The protein metabolism was calculated from the urinary nitrogen, and the nonprotein metabolism by application of the modified Zuntz-Schumberg [23] table to the observed nonprotein respiratory quotient. The calories were converted to grams of substances oxidized and the results were calculated in terms of twenty-four hours. Woodyatt's factors [24] for calculating the fatty acid-glucose ratio in grams and Shaffer's [25] factors for calculating the molecular ketogenic-antiketogenic ratio of the metabolized foodstuffs were used.

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22. Du Bois, E. F.: Basal Metabolism in Health and Disease, Philadelphia, Lee and Febiger, 1924, p. 71.

23. Zuntz, N., and Schumberg: Studien zu einen Physiologie des Marches, Berlin, 1901, p. 361. Lusk, G.: Analysis of the Oxidation of Mixtures of Carbohydrate and Fat—a Correction, J. Biol. Chem. **59**:41 (Feb.) 1924.

24. Formula of Woodyatt expressed in grams is:

$$\frac{\text{Fatty Acid}}{\text{Glucose}} = \frac{(0.46 \times \text{Protein}) + (0.9 \times \text{Fat})}{\text{Carbohydrate} + (0.58 \times \text{Protein}) + (0.1 \times \text{Fat})}$$

25. Formula of Shaffer, the constituents of which are expressed in grams is:

$$\frac{\text{Ketogens (gm. mol.)}}{\text{Antiketogens (gm. mol.)}} = \frac{(15 \times \text{Urinary Nitrogen}) + (3.43 \times \text{Fat})}{(5.56 \times \text{Carbo.}) + (20 \times \text{Urinary Nitrogen}) + (0.57 \times \text{Fat})}$$

CASE HISTORIES

The histories of the three normal children (E. F., L. A. and E. B.), the diabetic boy (F. A.) and the very obese but otherwise normal girl (S. A.) are summarized briefly in the first paper[16] of this series (Cases 2, 3, 4, 6 and 7, respectively). A more detailed account of the history of the patient with cyclic vomiting follows (Case 5 in the first paper):

CASE 5.—N. H., a girl, white, born Aug. 20, 1918, was admitted to the metabolism ward for study on April 7, 1925. She had been subject to attacks of vomiting from the age of 2 years, which recurred at intervals of two to four weeks, and lasted for six to seven days. During these attacks, which were always associated with respiratory infections, listlessness, anorexia and persistent vomting were present. The last one occurred during the week of March 9, 1925, at which time acetone was present in her urine and breath.

The patient's state of nutrition was below normal, and her tonsils were hypertrophied and diseased. The Wassermann and tuberculin reactions were negative. Metabolic studies were carried out for a period of one and one-half months. When they were ended, her tonsils and adenoids were removed. She is being followed in the outpatient department and her diet is under regulation. Up to the time of writing (November, 1925), she has had no return of the cyclic vomiting. Her appetite is excellent and she has gained weight. This child represents in a classical manner the group commonly known as "cyclic vomiters."

RESULTS

The details of the calorimeter observations appear in Table 1.

1. *The Ketogenic Balance of the Oxidized Foodstuffs in Relation to Ketonuria.*—Table 2 shows that the relation of the excretion of acetone bodies (in the urine) to the ketogenic value of the oxidized foodstuffs was maintained at all levels of ketosis. It was not significantly altered in the patient subject to cyclic vomiting (Case 5). The results are presented graphically in Charts 1 and 2.

The abnormal excretion of ketone bodies occurred, however, in five of the six children (Case 4 excepted) at fatty acid glucose ratios of 1.0 or lower (ketogenic-antiketogenic ratios of less than 0.7). In fact, keto-acids first appeared in the urine of all the children at fatty acid-glucose ratios of 0.7. These results are in marked contrast to those reported in the literature at the borderline of ketogenesis in adults. All observers,[1, 2, 3, 4] agree that in them a significant ketonuria rarely occurs at fatty acid-glucose ratios of less than 1.5 (ketogenic-antiketogenic ratios below 1.0).

Confirmatory evidence appears in Table 3. By use of Shaffer's formula (Footnote 1, reference 3), the expected excretion of total beta-oxybutyric acid was calculated by multiplying the excess of ketogenic over antiketogenic millimols in the metabolic mixture by 104 (the molecular weight of the acid). For our purpose, we assumed that any excess over a molecular ketogenic-antiketogenic ratio of 1.0 would result

in the production of ketone bodies at all levels of ketosis, in place of the ratio of 2.0 at the higher levels recommended by Shaffer. The expected beta-oxybutyric acid was compared to that actually excreted in the urine.

TABLE 2.—*Ketogenic Balance Calculated from the Calorimeter Data; the Respiratory Quotient; Relation to Excretion of Acetone Bodies*

	Date	Dietary F. A. to G.	Respiratory Quotient	Ratio of Gm. F. A. to G.†	Ratio of Molecules Keto-Acid to G.‡	Total Acetone Bodies per 24 Hours in Calorimeter Specimen
Case 2	Jan. 13	S.*	0.87	0.3	0.2	0.0
	Jan. 14	S.	0.82	0.6	0.4	0.34
	Jan. 2	S.	0.81	0.6	0.4	0.0
	Jan. 14	S.	0.78	1.0	0.8	2.95
	Jan. 3	S.	0.78	1.0	0.7	2.17
	Jan. 15	S.	0.78	1.1	0.8	2.71
	Jan. 16	S.	0.74	1.8	1.4	5.77
	Jan. 27	0.4	0.85	0.4	0.3	0.0
	Jan. 28	2.0	0.84	0.6	0.3	1.94
	Jan. 29	2.0	0.80	0.7	0.6	2.75
	Jan. 30	2.0	0.78	1.0	0.8	3.81
Case 3	Jan. 21	S.	0.91	0.2	0.1	0.0
	Jan. 23	S.	0.78	1.0	0.7	1.09
	Jan. 22	S.	0.78	1.1	0.8	3.64
	Jan. 22	S.	0.75	1.6	1.2	1.10
Case 4	Feb. 18	0.5	0.84	0.5	0.3	0.0
	Feb. 20	0.5	0.86	0.4	0.3	0.0
	Feb. 25	1.5	0.83	0.5	0.4	0.32
	March 2	2.0	0.78	1.0	0.8	0.05
	March 4	2.5	0.80	0.8	0.6	0.35
	March 5	2.5	0.79	0.9	—	—
	March 6	2.5	0.79	0.9	0.7	0.40
	March 7	2.7	0.77	1.1	0.9	0.46
Case 5	May 13	S.	0.85	0.4	0.2	0.0
	May 14	S.	0.85	0.5	0.4	0.70
	May 15	S.	0.76	1.4	1.0	1.44
	May 16	S.	0.76	1.3	0.9	5.87
	April 15	0.5	0.85	0.4	0.3	0.45
	April 21	1.0	0.78	1.1	0.8	1.90
	April 24	1.5	0.78	1.1	0.8	4.06
	April 25	1.5	0.77	1.2	0.9	3.47
	April 29	2.0	0.76	1.4	1.0	8.43
Case 6	May 8	S.	0.81	0.7	0.5	0.0
	May 9	S.	0.79	0.9	0.7	0.21
	May 10	S.	0.80	0.7	0.7	1.15
	May 11	S.	0.76	1.5	0.9	2.13
	April 14	1.1	0.80	0.8	0.5	0.0
	April 17	0.8	0.79	0.9	0.6	0.0
	April 22	1.6	0.78	1.0	0.7	0.27
	April 27	2.0	0.79	0.9	0.6	0.0
	April 30	2.5	0.79	0.8	0.6	0.11
Case 7	May 18	S.	0.83	0.5	0.3	0.0
	May 19	S.	0.80	0.7	0.5	0.16
	May 20	S.	0.77	1.1	0.8	5.86
	May 21	S.	0.76	1.4	0.9	11.31

* S indicates starvation.
† Woodyatt's factors.
‡ Shaffer's factors.

Although the modified assumption markedly increased the expected ketone production, and although the acetone eliminated by the breath was not considered, the actual excretion of keto-acids greatly exceeded the expected output in every instance except one (Case 3, second observation of January 22, Table 3).

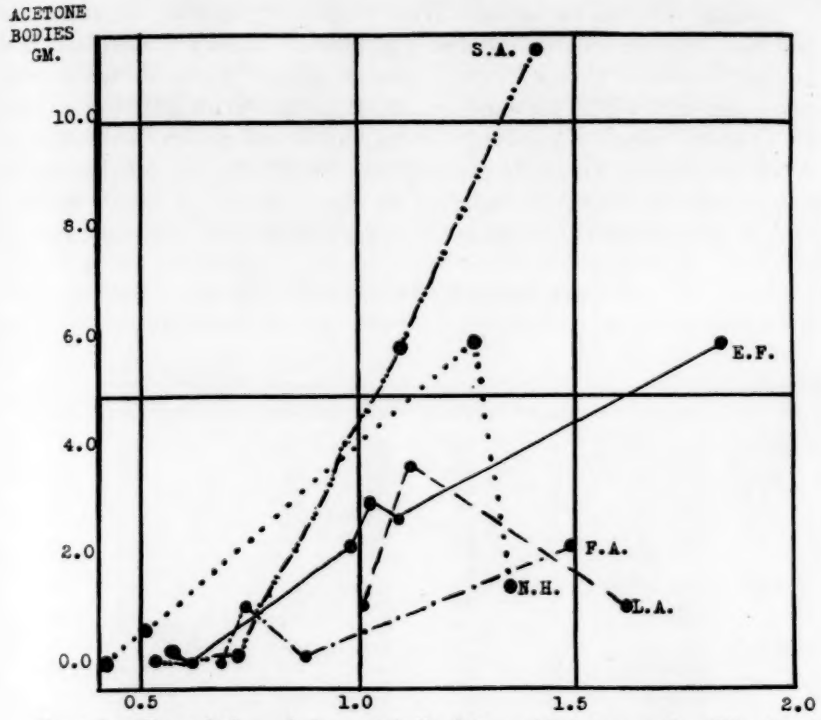

Chart 1.—The relation of the metabolic fatty acid-glucose ratio (Woodyatt) to the excretion of acetone bodies during starvation.

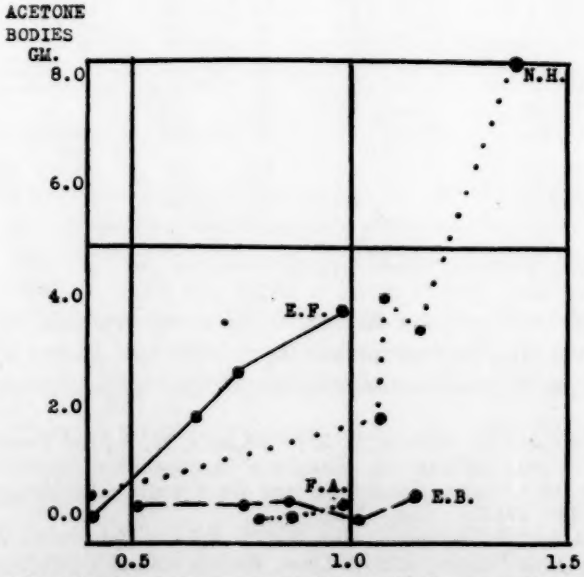

Chart 2.—The relation of the metabolic fatty acid-glucose ratio (Woodyatt) to the excretion of acetone bodies during ingestion of low carbohydrate, high fat diets.

Similar calculations of data from respiratory studies on adults by McCann, Hannon, Perlzweig and Tompkins,[26] and by Richardson and Levine [27] showed that in every instance except four, in which discrepancies were slight, the expected output of keto-acids greatly exceeded the quantity actually excreted (twenty observations on nine adults). While respiratory quotients are not entirely reliable for calculating the proportions of foodstuffs oxidized in the presence of severe ketosis, Lusk [28] deduced that the final error is not considerable (the final change

TABLE 3.—*Ketogenic Balance in Ketosis*

	Date	Diet *	Ratio K. to A.	Ketogenic Millimols	Antiketogenic Millimols	Excess Ketogenic Millimols	Total Hydroxibutyric Acid in Urine	
							Expected, Gm.	Found,† Gm.
Case 2	Jan. 14	S.	0.4	241	582	—	0.0	0.61
	Jan. 14	S.	0.8	270	356	—	0.0	5.29
	Jan. 3	S.	0.7	350	480	—	0.0	3.80
	Jan. 15	S.	0.8	310	389	—	0.0	4.86
	Jan. 16	S.	1.4	348	254	94	9.78	10.35
	Jan. 28	D.	0.3	222	666	—	0.0	3.48
	Jan. 29	D.	0.6	290	513	—	0.0	4.93
	Jan. 30	D.	0.8	339	449	—	0.0	6.83
Case 3	Jan. 23	S.	0.8	286	383	—	0.0	1.95
	Jan. 22	S.	0.8	299	369	—	0.0	6.53
	Jan. 22	S.	1.2	278	228	50	5.20	1.97
Case 4	Feb. 25	D.	0.4	242	617	—	0.0	0.57
	March 2	D.	0.8	294	376	—	0.0	0.09
	March 4	D.	0.6	295	508	—	0.0	0.63
	March 6	D.	0.7	322	488	—	0.0	0.72
	March 7	D.	0.9	366	426	—	0.0	0.82
Case 5	May 14	S.	0.4	225	588	—	0.0	1.26
	May 15	S.	1.0	286	292	—	0.0	2.58
	May 16	S.	1.0	304	324	—	0.0	10.52
	April 15	D.	0.3	213	719	—	0.0	0.81
	April 21	D.	0.8	314	404	—	0.0	3.41
	April 24	D.	0.8	282	355	—	0.0	7.28
	April 25	D.	0.9	331	389	—	0.0	6.22
	April 29	D.	1.0	370	367	3	0.3	15.11
Case 6	May 9	S.	0.7	528	756	—	0.0	0.38
	May 10	S.	0.7	709	1061	—	0.0	2.06
	May 11	S.	0.9	630	722	—	0.0	3.82
	April 22	D.	0.7	305	409	—	0.0	0.49
	April 30	D.	0.6	301	484	—	0.0	0.19
Case 7	May 19	S.	0.5	346	677	—	0.0	0.29
	May 20	S.	0.8	438	555	—	0.0	10.51
	May 21	S.	0.9	463	494	—	0.0	20.40

* S. indicates starvation; D, diet.
† Obtained by multiplying acetone bodies as acetone by 1.793.

in the respiratory quotient is from 0.707 to approximately 0.715). In only a few of the observations was the excretion of ketone bodies in the urine sufficient to question the reliability of the respiratory quotients.

26. McCann, W. S.; Hannon, R. R.; Perlzweig, W. A., and Tompkins, E. H.: Studies of Diabetes Mellitus. II. Results of Treatment by Diet Adjustment with Reference to Maintenance Requirement and the Ketogenic-Antiketogenic Balance, Arch. Int. Med. **32**:226 (Aug.) 1923.

27. Richardson, H. B., and Levine, S. Z.: Clinical Calorimetry 37; Infection and the Ketogenic Balance, J. Biol. Chem. **63**:465 (March) 1925.

28. Lusk, G.: Clinical Calorimetry. On the Diabetic Respiratory Quotient, Arch. Int. Med. **15**:939 (May) 1915.

The experimental evidence is, therefore, in complete accord with clinical observations of the greater sensitiveness of children to ketosis. In order to explain the relatively higher keto-acid excretion of children, one of two assumptions may be made. We may either accept the theory of the ketogenic balance and explain the discrepancy by modifying the values ascribed to the ketogenic and antiketogenic factors for adults, or we may assume, with Allen,[7] the influence of a special biologic factor in ketosis not explicable solely on the mechanism of the ketogenic balance. The data are inadequate to evaluate their relative importance. Whatever the explanation, the fact that children are more sensitive than adults to ketosis is conclusively demonstrated.

TABLE 4.—*Blood Sugar, Carbon Dioxid Content and Acetone During Starvation*

	Date	Fasting Hours	Blood Sugar (W. B.) Mg. per 100 Cc.	CO_2 Content (W. B.) Percentage by Volume	Acetone (W. B.) Mg. per 100 Cc.
Case 2	Jan. 13	4:05	80.4	49.4	—
	Jan. 14	24:25	86.5	44.0	—
	Jan. 3	43:45	65.3	33.5	—
	Jan. 16	73:00	59.6	22.2	—
	Jan. 16*	78:35	89.5	19.6	52.4
Case 3	Jan. 21	4:10	107.0	49.3	—
	Jan. 22	30:20	57.5	32.6	—
	Jan. 22	35:10	68.5	33.5	—
	Jan. 23	57:25	42.7	24.0	34.1
Case 5	April 15	6:30	77.2	41.7	—
	May 14	28:55	82.1	36.7	—
	May 15	52:15	45.4	37.8	—
	May 16	75:45	56.6	32.6	34.7
Case 7	May 19	32:10	89.0	55.9	—
	May 20	53:10	55.2	38.7	57.7
	May 21	80:40	64.0	30.2	63.3
Case 6	May 8	3:50	77.3	53.6	—
	May 9	30:40	74.4	45.3	—
	May 11	80:20	60.8	35.8	—

* Blood was obtained with difficulty.

2. *The Sugar and Carbon Dioxide of the Blood During Ketosis.*—Tables 4 and 5 show that the sugar and carbon dioxide content of the blood fall steadily during complete fasting and during partial carbohydrate starvation (high fat diets). These results are comparable to those of other workers except that, contrary to the observation of Ross and Josephs,[11] the blood sugar failed to reach a minimum sooner in the child with cyclic vomiting than in the normal children.

3. *The Relation of the Oxidized to the Ingested Foodstuffs.*—In Table 6, the foodstuffs ingested are compared to the foodstuffs oxidized, as calculated from the calorimeter data in terms of twenty-four hours. Table 7 shows the resulting dietary and metabolic fatty acid-glucose ratios, computed from Table 6 by use of Woodyatt's factors.

The tables show that when the carbohydrate content of the maintenance diets was ample, the fatty acid glucose ratios of the foodstuffs in the metabolic mixtures and in the diets were the same. However, as the proportions of fat to carbohydrate in the diets were raised without

TABLE 5.—*Blood Sugar and Carbon Dioxide on Diets with Different Dietary Ratios*

	Date	F. A. : G. Diet	Days on Diet	Blood Sugar (W. B.) Mg. per 100 Cc.	CO_2 Content (W. B.) Percentage by Volume
Case 2	Jan. 27	0.4	11	100.0	44.5
	Jan. 28	2.0	1	54.4	43.1
	Jan. 29	2.0	2	57.8	33.5
	Jan. 30	2.0	3	52.5	30.9
	Jan. 6	3.0	2	37.5	25.7
Case 4	Feb. 18	0.5	3	92.4	45.3
	Feb. 25	1.5	5	73.6	40.5
	March 2	2.0	5	79.9	40.3
	March 4	2.5	2	65 5	—
*	March 4	2.5	2	55.1	41.6
Case 5	April 15	0.5	5	77.2	41.7
	April 21	1.0	5	68.2	40.7
	April 25	1.5	4	74.0	—
	April 29	2.0	4	58.4	30.9
Case 6	April 17	0.8	3	93.5	43.8
	April 14	0.9	4	90.9	53.9
	April 22	1.6	5	71.5	50.0
	April 27	2.0	5	75.0	48.7
	April 30	2.5	3	69.9	52.1

* Before and after calorimeter observation, three hours apart.

TABLE 6.—*Food Eaten Compared with Food Oxidized Per Twenty-four Hours*

			Diet				Metabolized			
Case	Date	No. Days	Protein, Gm.	Fat, Gm.	Carbohydrate, Gm.	Calories, Total	Protein, Gm.	Fat, Gm.	Carbohydrate, Gm.	Calories, Total
2	Jan. 30	3	45.7	94.1	16.7	1,131	50.4	64.5	46.7	998
4	Feb. 18	3	25.1	52.1	100.1	998	29.6	50.1	107.4	1,028
	Feb. 20	5	25.1	52.1	100.1	998	28.9	37.7	105.1	900
	Feb. 25	5	50.0	70.2	19.9	939	47.1	38.7	80.7	883
	March 2	5	50.0	80.0	10.0	990	45.2	55.0	36.8	848
	March 4	2	50.0	85.0	2.0	1,004	50.3	52.0	58.2	929
	March 5	3	50.0	85.0	2.0	1,004	52.2	55.5	48.3	928
	March 6	4	50.0	85.0	2.0	1,004	52.5	58.2	52.5	971
	March 7	1	50.0	86.0	0.3	1,006	52.2	71.4	40.3	1,043
5	April 15	5	35.0	42.0	90.0	903	25.4	44.9	110.6	975
	April 21	6	40.0	60.0	44.0	902	26.9	73.4	50.1	998
	April 24	3	45.0	72.0	24.0	953	31.7	60.7	39.9	858
	April 25	4	45.0	72.0	24.0	953	33.8	73.6	43.4	1,002
	April 29	4	50.0	76.0	10.0	953	38.4	81.9	36.2	1,067
6	April 17	3	40.0	60.0	60.0	968	38.4	58.9	51.3	915
	April 14	4	40.0	78.0	50.0	1,094	35.9	54.8	56.6	889
	April 22	5	47.0	74.0	22.0	971	48.9	56.0	40.6	888
	April 27	5	50.0	78.0	10.0	971	27.9	63.3	56.1	983
	April 30	3	52.0	82.0	0.0	976	42.7	59.0	57.1	968

affecting materially the total calories, the similarity of the dietary and metabolic ratios was no longer evident. The two normal children (Case 2 and Case 4) and the diabetic boy (Case 6) oxidized more carbohydrate and less fat than they received in their diets. This resulted in consistently lower metabolic than dietary fatty acid-glucose ratios, the

discrepancy becoming more marked as the ketogenic value of the diets was raised. Stored carbohydrate displaced to a marked extent the ingested fat from the metabolic mixtures of these children. Differences between dietary and metabolic ratios were considerably less in the child with cyclic vomiting (Case 5) than in the normal children. This child tended to burn all of the fat contained in the diet (Table 6). The extent to which stored carbohydrate displaced ingested fat from the metabolic mixture of this child was distinctly limited. It is noteworthy that the caloric value of all diets approximated the heat production, as determined in the respiration chamber, and was just sufficient to cover

TABLE 7.—*Dietary and Metabolic Ratios*

	Date	F. A. : G. Ratio (Woodyatt)	
		Dietary	Metabolic
Case 2	Jan. 30	2.0	1.0
Case 4	Feb. 18	0.5	0.5
	Feb. 20	0.5	0.4
	Feb. 25	1.5	0.5
	March 2	2.0	1.0
	March 4	2.5	0.8
	March 5	2.5	0.9
	March 6	2.5	0.9
	March 7	2.7	1.1
Case 5	April 15	0.5	0.4
	April 21	1.0	1.1
	April 24	1.5	1.1
	April 25	1.5	1.2
	April 29	2.0	1.4
Case 6	April 17	0.8	0.9
	April 14	1.1	0.8
	April 22	1.6	1.0
	April 27	2.0	0.9
	April 30	2.5	0.8

TABLE 8.—*Relation of the Proportions of Ingested to Metabolized Foodstuffs*

		Diet *					Metabolized †				
			% Calories from					% Calories from			
Case	No. of Days	Total Calories	Protein	Fat	Carbohydrate	Date of Observation	Total Calories	Protein	Fat	Carbohydrate	R. Q.
2	5	1,907	11.6	38.0	50.4	Jan. 13	992	10.7	33.8	55.5	0.87
3	13	1,350	10.4	34.8	54.8	Jan. 21	935	8.9	23.3	67.8	0.91
4	6	2,014	15.2	49.1	35.7	March 13	902	14.5	5.7	79.8	0.95
5	14	1,447	9.9	40.5	49.6	May 13	761	11.5	43.3	45.2	0.85

* All observations were begun five to six hours after the last meal.
† The last meal consisted of one-sixth of the total daily diet.

the maintenance requirement. Differences between dietary and metabolic proportions were due, therefore, not to excessive caloric intake, but to actual replacement in the metabolic mixture of ingested fat by stored carbohydrate.

The relative proportions of carbohydrate and fat oxidized by the three normal children and the child with cyclic vomiting following extended periods of high carbohydrate, high caloric feeding, was also determined by means of the respiration chamber. The results appear in Table 8.

The patient subject to cyclic vomiting (Case 5) utilized a greater proportion of fat, and, conversely, a smaller proportion of carbohydrate than the three normal children, although the diets of all contained an approximately equal excess of carbohydrate.

To show that the slight variations in activity did not affect appreciably the respiratory quotients, and that they could, therefore, be excluded as a cause of the differences shown in Tables 7 and 8, the results of seven pairs of equivalent experiments on three children during fasting, high carbohydrate, and high fat feeding are compared in Table 9.

Restricted activity did not alter consistently the proportions of foodstuffs oxidized by the normal children and by the child with cyclic vomiting under more nearly basal conditions, as evidenced by its minimal effect on the respiratory quotients. With more strenuous exercise,

TABLE 9.—*The Effect of Mild Activity on the Respiratory Quotient*

	Date	Calories per 24 Hours	Respiratory Quotient	Ratio F. A. : G.	Remarks *
Case 2	Jan. 13	992	0.87	0.3	Active } Dietary F. A. : G.
	Jan. 27	936	0.85	0.4	Inactive } ratio = 0.35
	Jan. 30	998	0.78	1.0	Active } Dietary F. A. : G
	Jan. 29	942	0.80	0.7	Inactive } ratio = 2.01
	Jan. 3	1,088	0.78	1.0	Active } Fasting 42 hours
	Jan. 14	848	0.78	1.0	Inactive } 37 hours
Case 4	Feb. 18	1,028	0.84	0.5	Active } Dietary F. A. : G.
	Feb. 20	900	0.86	0.4	Inactive } ratio = 0.49
	March 6	971	0.79	0.9	Active } Dietary F. A. : G.
	March 5	928	0.79	0.9	Inactive } ratio = 2.52
Case 5	April 15	975	0.85	0.4	Dietary F. A. : G. ratio Active } = 0.47
	May 13	761	0.85	0.4	Inactive } = 0.36
	April 25	1,002	0.77	1.2	Active } Dietary F. A. : G.
	April 24	858	0.78	1.1	Inactive } ratio = 1.49

* All calorimeter observations were begun four to six hours after the last meal.

Richardson and Levine [29] obtained an elevation of the respiratory quotients in normal adults and a depression in diabetic patients.

The results, though based on a limited number of cases, are consistent. They suggest the following:

RESULTS

1. Children do not necessarily oxidize foodstuffs in the proportions contained in the diet. This fact renders dietary studies unsuitable for correlating the ketogenic balance with the keto-acid production. It may also explain the relatively trivial ketosis often present while on the excessively high fat diets recommended by Marsh and Newburgh [30] in

29. Richardson, H. B., and Levine, S. Z.: The Effect of the Exercise on the Respiratory Quotient in Diabetes, 1925. (In preparation.)

30. Newburgh, L. H., and Marsh, P. L.: The Use of a High Fat Diet in the Treatment of Diabetes Mellitus, Arch. Int. Med. **26**:647 (Dec.) 1920.

the treatment of diabetes. In work on adults, Richardson and Ladd [3] have previously pointed out similar findings.

2. Normal children vary in the relative extent to which they utilize the different foodstuffs. They have in common, however, the fact that carbohydrate, irrespective of its source, displaces fat from the metabolic mixture, relegating it presumably to the tissues for storage. Expressed in another way, normal children ordinarily are "carbohydrate burners." [31]

3. As indicated from the data on one case, the replacement of fat by carbohydrate in the metabolic mixture seems to be distinctly limited in patients subject to cyclic vomiting. Expressed in other terms, they are nearly as marked "fat burners" as "carbohydrate burners,[32] which may explain their hypersusceptibility to ketosis.

CLINICAL DATA DURING THE EXPERIMENTAL KETOSIS

No typical attack of cyclic vomiting was induced by raising the dietary ratio. When it reached 1.0, however, the patient with cyclic vomiting (Case 5) showed some listlessness and irritability, and the urine and breath contained large amounts of acetone. At a dietary F.A.: G. ratio of 2.0, dizziness, restlessness and marked drowsiness supervened. After five days on this diet, the foregoing symptoms were quite marked and the urinary acetone was 4 plus qualitatively. The administration of orange juice and glucose cleared up the symptoms entirely within twelve hours. Clinical manifestations of ketosis were less marked during fasting than while on the high fat diets.

The two normal girls (Cases 2 and 3) presented clinically less evidence of ketosis than the child with cyclic vomiting during both fasting and high fat periods. The obese girl (Case 7) showed a more notable ketosis than the other three girls during fasting. The normal boy (Case 4) and the diabetic boy (Case 6) were in no way affected, being happy and active throughout the experimental periods.

The severity of the ketosis, as judged clinically, was comparable in every case to the extent of the ketone body excretion in the urine.

COMMENT

Technic.—The results showing the relation of the metabolic ketogenic balance to the excretion of ketone bodies in the urine are based on

31. Experiments with diets begun by Weymuller in 1922, the results of which are soon to be published from this laboratory, indicated strongly the probability of fat storage by normal children and to a lesser degree by children especially subject to ketosis. In many instances, considerably less ketone bodies were excreted in the urine than were expected on the basis of Shaffer's calculations.

32. The lower carbohydrate utilization in the child studied did not result from a diminished glycogen storage. This is shown in fasting experiments reported in a communication (to be published subsequently) which indicate as efficient storage in this child as in the normal children.

calorimeter observations of two to four hours' duration. It was assumed that calculation of the data in terms of twenty-four hours, in order to compare dietary and metabolic ratios, did not introduce an appreciable error. Observations were made only after the children had been on the same diets for at least three days. The higher and lower levels of the metabolism for the day and night were reproduced by dividing the observations into quiet and relatively active periods. The respiratory quotients in these periods of varying activity were essentially the same. This fact, together with their similarity in equivalent experiments at all times of the day and part of the night (up to 12:10 a. m.) is good evidence that the relative proportions of foodstuffs in the metabolic mixtures did not vary appreciably throughout the twenty-four hours of the day and night. Richardson and Ladd [3] found only a slight change in the quotients of a diabetic patient in two similar experiments (0.74 to 0.75), one being made in the afternoon and the other being repeated at midnight, thirty-six hours later.

Not only was the respiratory metabolism constant for all parts of the day, but the acetone excretion was also uniform, as shown by the close parallelism between the total daily acetone excretion in the urine and the quantities in the calorimeter specimen when calculated for twenty-four hours. The relation of the metabolic fatty acid-glucose ratio to the excretion of ketone bodies was also maintained at all times of the day.

Respiratory Quotient.—Only the average respiratory quotients in observations of two or more hours were used to calculate the proportions of foodstuffs oxidized. They are, however, also recorded for individual periods to note the hourly fluctuations (Table 1). The fifth column of this table shows that the maximum variations of quotients for both quiet and active periods exceeded 0.03 (0.04 to 0.07) in only fifteen of the forty-five observations; the maximum range being between 0.0 and 0.03 in the other thirty instances. Deviations of the hourly quotients from the average for entire observations were notably less than this, being more than 0.03 in only three instances. The consistent results indicate that, from a technical standpoint, the average respiratory quotients in these determinations of two or more hours represent accurately the proportions of foodstuffs oxidized during the periods of observations. The technical accuracy of the method is also demonstrated by the results of the alcohol checks.[16] Theoretic objections to the use of respiratory quotients for calculating the oxidizing foodstuffs have been fully discussed by Lusk,[33] by Loebel, Barr, Tolstoi and Himwich,[34]

33. Lusk, G.: Die Energiequelle bei der Muskelarbeit, Biochem. Ztschr. **156:** 334, 1925.

34. Loebel, R. O.; Barr, D. P.; Tolstoi, E., and Himwich, H. E. Studies of the Effect of Exercise in Diabetes, II. Lactic Acid Formation in Phlorizin Diabetes, J. Biol. Chem. **61:**9 (Aug.) 1924.

by Richardson and Ladd [3] and by Richardson and Levine.[29] Their discussion includes a presentation of the European theory [35] of the conversion of fat to carbohydrate and their reasons for questioning it. It suffices to state here that all the before-mentioned observers have advocated the procedure as reliable, providing that the respiratory quotients are obtained over periods of two or more hours, and that no changes in the fixed acid of the blood occur during observations.

Results.—The results suggest that the factors for calculating the ketogenic balance in adults, as formulated by Shaffer and Woodyatt, may need revision to be strictly applicable to children. Children ordinarily require the simultaneous oxidation of relatively more ketolytic to ketogenic substances than adults, in order that the accumulation of intermediary ketone bodies may with certainty be prevented. This may be the factor which makes children especially sensitive to ketogenesis. Observations on this lower ketogenic threshold are too few to establish quantitative relations.

The patient with cyclic vomiting (Case 5) showed no significant change from normal children in the relation of the metabolic ketogenic balance to ketone body excretion. Neither could the hypersusceptibility of this child to ketosis be accounted for by an increased basal metabolism.[16] Furthermore, it was not due apparently to a diminshed capacity for storing glycogen.[36] The tendency of this child to oxidize fat almost as readily as carbohydrate is advanced as a tentative explanation. In normal children, carbohydrate, if available, displaces fat from the metabolic mixture.

The experiments on this one child subject to cyclic vomiting were made only between attacks and under maintenance conditions. Further work is planned to study the condition during attacks and during vigorous exercise, and to determine whether these observations can be duplicated in other children affected with the same condition. It is conceivable, of course, that different factors may be operative in different persons which may interfere with ketolysis and thereby induce ketosis. This question can be answered only by extended investigation.

SUMMARY AND CONCLUSIONS

The results are based on data derived from measurements of the respiratory exchange of six children during the ketosis induced by fasting and by administration of low carbohydrate, high fat diets. They suggest that:

35. Krogh, A., and Linhard, J. The Relative Value of Fat and Carbohydrate as Sources of Muscular Energy, Biochem. J. **14**:290 (July) 1920.

36. Levine, S. Z., and Wilson, J. R.: The Respiratory Metabolism in Infancy and Childhood. III. Glycogen Storage 1925. (In press.)

1. Respiratory quotients obtained in well-controlled calorimeter determinations of two to four hours, represent accurately the proportions of foodstuffs oxidized during the periods of observation.

2. A significant ketonuria appears in children at consistently lower metabolic fatty acid-glucose ratios than in adults. Furthermore, children excrete a relatively greater quantity of ketone bodies at a given metabolic ratio above the threshold of ketosis. This fact may explain the more rapid development and the greater severity of ketosis in children than in adults.

3. The relation of the metabolic ketogenic balance to the keto-acid excretion was not significantly altered in the patient subject to cyclic vomiting. The evidence suggests, therefore, that this factor may be minimized as a cause of the exaggerated tendency to ketosis exhibited by this group of children.

4. Children do not necessarily oxidize foodstuffs in the proportions contained in the diet. This fact renders dietary data unreliable in correlating the ketogenic balance with ketone body excretion.

5. Normal children usually oxidize a higher proportion of carbohydrate and a lower proportion of fat than they receive in their diets. The discrepancy is most marked when the fat content of the diet is relatively high.

6. The tendency to oxidize carbohydrate at the expense of fat was less apparent in the child with cyclic vomiting than in the control cases. We offer this as a tentative explanation for the increased susceptibility of these children to ketosis.

7. The sugar and carbon dioxide content of the blood fall during fasting and during the ingestion of low carbohydrate, high fat diets. The rate of fall was the same in the child with cyclic vomiting as in the normal children.

8. Clinically, the tendency of children to develop ketosis may logically be counteracted by giving diets high in carbohydrate and low in fat, especially in conditions associated with an elevated metabolism. Such routine diets would seem to be especially indicated in the group of children who are subject to attacks of cyclic vomiting associated with ketosis, in an effort to reduce the number and possibly the severity of the attacks.

The evidence adduced from the data is in accord with the clinical observation that children are particularly sensitive to ketogenesis. It also suggests a tentative explanation for the exaggeration of this tendency in the group of children, known clinically as "cyclic vomiters."

AURICULAR FIBRILLATION

REPORT OF CASE IN A CHILD AGED FOUR YEARS *

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AND
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We desire to place on record a case of auricular fibrillation occurring in a child, aged 4 years. So far as we have been able to determine, this is the youngest patient hitherto reported. The data concerning the previous instances in which auricular fibrillation has been detected in children aged 10 years or less are recorded in the table.

It is apparent that rheumatic heart disease is the most common etiologic factor in the causation of auricular fibrillation in these young children, as it is in young adults.

Data of Previous Instances of Auricular Fibrillation

Case	Author	Age of Patient, Years	Type of Heart Disease
1	Price and Mackenzie (Heart **3**: 233, 1911-1912).....	9	Diphtheritic
2	Sutherland and Coombs (Heart **5**: 15, 1913-1914).....	5	Rheumatic
3	Ehrenreich (New York M. J. **99**: 269, 1914).....	9	Rheumatic
4	Ogden (Am. J. Dis. Child. **29**: 767, 1925).....	10	Rheumatic
5	Present	4	Probably rheumatic

CASE REPORT

History.—C. S., a boy, aged 4 years, was first seen in the Dispensary of the Harriet Lane Home, on Sept. 10, 1924. He was "blue" at birth and had to be resuscitated; but thereafter for a year he was apparently normal. At this time, he began to have coughing spells, during which he became very cyanotic, and his parents were told by a physician that he had heart trouble. During the next three years he had frequent paroxysms of coughing, there was apparently slight dyspnea on exertion, and he was never as active as the average child of his age. At the age of 2½ years, he had a severe sore throat. There was no history of chorea, joint pains, or other acute illnesses. For the last year, there had been precordial pain, and during the last three months, the dyspnea became considerably more marked and the abdomen swollen.

At the first examination, he was found to be quite irritable, and his skin had a pasty appearance. The heart was enlarged, the apex beat being in the sixth interspace in the anterior axillary line. There was a systolic murmur at the apex, and there was a marked irregularity of the heart action, thought to be due to sinus irregularity and extrasystoles. No graphic records were taken. Otherwise, the examination was essentially negative.

Because he became worse during the next two weeks, he was admitted to the hospital on September 25. On this occasion, his face was puffy and there was slight edema of the lower extremities. There was marked dyspnea and

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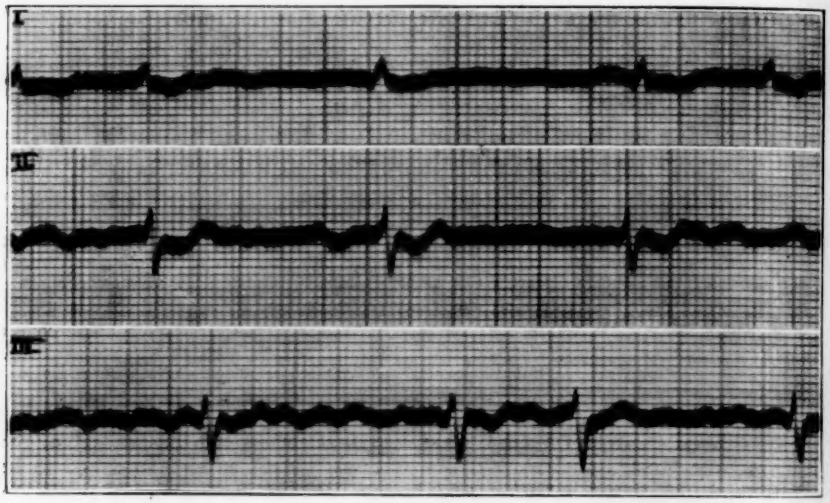
* From the Medical and Pediatric Departments of the Johns Hopkins Hospital and University.

orthopnea, the skin was pale and the mucous membranes were slightly cyanotic. The tonsils were very large. At the left base of the lungs, the breath sounds had a slightly tubular quality. The heart was enlarged to about the same extent as had been observed previously; there was a thrill at the apex, difficult to time on account of the rapid heart rate, about 160 per minute, and a short systolic murmur was heard at the apex. The rhythm of the heart was quite irregular, due, it was thought, either to numerous extrasystoles or to auricular fibrillation. There was tenderness over the liver, which was enlarged, and the spleen was palpable just below the costal margin.

The white blood cells were 11,400 per cubic millimeter; the hemoglobin was 80 per cent. The urine contained a small amount of albumin and a few casts.

Two days later, after the administration of 1.2 gm. of digitalis, the patient was distinctly improved. The heart rate was now about 80 per minute and the systolic apical murmur was almost imperceptible. It was also noted that the size of the heart was definitely smaller. The heart sounds remained clear thereafter.



Electrocardiogram (leads I, II and III) taken on October 2, showing auricular fibrillation and probably incomplete right bundle branch block (due to digitalis?).

On October 2, the day on which he was discharged, an electrocardiographic record was taken.

This showed auricular fibrillation; the T waves were inverted in leads I and II. The QRS interval was 0.10 second, which, with the predominance of the levogram and the characteristic direction of the T waves, probably indicated the presence of right bundle branch block, possibly due to digitalis.

Throughout his short stay in the hospital, the patient's temperature varied between 96 and 98 F., being somewhat higher (up to 100 F.) during the first two days. He has not been seen by us since he was taken from the hospital, but we were informed by his mother that he remained quite well for six to seven months. During the next three months, he became progressively worse, edema and dyspnea becoming marked, and death finally ensuing rather suddenly. A necropsy was not obtained. A communication from his physician stated that on every occasion that he saw the child, the heart action was grossly irregular.

COMMENT

Excepting the presence of auricular fibrillation in a child as young as this, the chief interest in the case lay in determining the etiology of the heart disease. There was no evidence of congenital heart disease. The rapid increase in symptoms shortly before his admission, the transient murmurs, and the alterations in the size of his heart during a short interval of time, seemed to indicate that the child was suffering from acute myocarditis. At his age rheumatic fever is uncommon; yet Denzer [1] has reported the finding of rheumatic heart disease in patients under 2 years of age. In the absence of any other etiologic factor, and the history and evidence of tonsillitis, it is likely that rheumatic involvement of the myocardium was the cause of this child's heart disease, although no proof for this belief is at hand. It is impossible to be certain as to the duration of the arrhythmia. When the child was seen on September 10, it was noted that there was marked irregularity of the cardiac rhythm, the irregularity being ascribed to sinus arrhythmia associated with numerous extrasystoles. It is quite possible that the irregularity at this time was due to auricular fibrillation, which may have persisted up to the time of and throughout his stay in the hospital.

CONCLUSION

Undoubtedly, auricular fibrillation occurs more commonly in young children than one would suspect from the small number of cases which have hitherto been reported. The apparent rarity is probably due, in part at least, to the fact that this type of irregularity is not ordinarily considered in children, and, in the absence of graphic records, is quite naturally confused with sinus arrhythmia, perhaps associated with extrasystoles. The work of Cohn and Swift [2] has demonstrated how frequently transient disturbances of the cardiac mechanism occur in acute rheumatic fever.

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1. Denzer, B. S.: Rheumatic Heart Disease in Children Under Two Years of Age: Report of Three Cases, J. A. M. A. **82**:1243 (April 19) 1924.

2. Cohn, A. E., and Swift, H. F.: Electrocardiographic Evidence of Myocardial Involvement in Rheumatic Fever, J. Exper. Med. **39**:1 (Jan.) 1924.

INTRAVENOUS INJECTION OF HYPERTONIC SALT SOLUTION IN ACUTE POLIOMYELITIS

REPORT OF CASE *

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Aycock and Amoss [1] have reported the recovery of a patient having severe poliomyelitis, with an ascending paralysis which involved the respiratory muscles. As a last resort, they gave the patient an intravenous injection of hypertonic Ringer's solution and an intraspinal injection of serum from a convalescent patient.

The ideas which guided Aycock and Amoss in the development of their method of treatment were based on experimental and pathologic investigations. Weed and Hughson [2] had shown that "the intravenous injection of strongly hypertonic solutions causes a prolonged and profound fall in the pressure of the cerebrospinal fluid, preceded usually by a sharp rise." These investigators had noted also an actual shrinkage in the size of the brain and spinal cord following the intravenous injection, an observation which had suggested to them that such treatment might cause an aspiration of materials from the subarachnoid space into the perivascular lymph spaces of the nervous tissue. Furthermore, pathologists had found that in poliomyelitis a marked inflammatory edema surrounds those areas of the brain and cord which are the chief seat of injury. It seemed reasonable to suppose that the increased pressure on the nervous tissues, resulting from the development of the inflammatory process in a closed space, was in large part the cause of the paralyses which are present in the acute stage of the disease but which ultimately disappear. If, at the critical moment of the disease, the pressure resulting from the inflammation could be diminished, the acute situation might successfully be passed and the life of the patient be saved. Aycock and Amoss [3] had performed experiments which suggested that the inflammatory edema in the spinal cords of monkeys with poliomyelitis had responded to a combined treatment of serum and intravenous hypertonic saline solution in a more satisfactory manner than to injections of serum alone, which had been employed in the control animals.

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* Received for publication, Oct. 16, 1925.

* From the Department of Pediatrics, Yale University, School of Medicine and the Pediatric Service, New Haven Hospital.

1. Aycock, W. L., and Amoss, H. L.: The Treatment of Acute Poliomyelitis, J. A. M. A. **81**:474 (Aug. 11) 1923.

2. Weed, L. H., and Hughson, W.: Am. J. Physiol. **58**:53 (Nov.) 1921.

3. Aycock, W. L., and Amoss, H. L.: Bull. Johns Houkins Hosp. **34**:361 (Nov.) 1923.

The patient of Aycock and Amoss was a boy, aged 4 years. He showed marked general flaccid paralysis, including paralysis of the intercostal muscles. Respiration was difficult and the cough was feeble. The patient was treated in the following way:

> . . . lumbar puncture was performed; 35 c.c. of clear spinal fluid was removed, and human convalescent poliomyelitic serum allowed to flow in until equilibrium was established with a head of 4 inches. It was estimated that 20 c.c. of serum flowed into the subarachnoid space. While the needle and connections remained in place, there was injected, intravenously under ether anesthesia, 25 c.c. of concentrated Ringer's solution, of which the sodium chlorid content was 18 per cent. Within two minutes, the serum began to flow again into the spinal canal at a fairly rapid rate. After 20 c.c of serum had been allowed to flow in, there was no apparent decrease in the rate of flow, and the needle was withdrawn. Since there was already obvious involvement of the respiratory center, the injections were made with dispatch, and no manometric readings were made.

The patient of Aycock and Amoss was slightly worse on the day following treatment, then gradually recovered.

I wish to report the case of a patient with a similar clinical picture, who was treated with intravenous injections of hypertonic saline solution, but without intraspinous serum treatment.

REPORT OF CASE

E. B., a boy, aged 5 years, whose past history was irrelevant, was admitted to the Pediatric Service of the New Haven Hospital on Nov. 20, 1923. He became ill about one week before admission with "a cold." Nasal discharge, cough and slight fever were present. Four days before admission there were "chills and fever." These symptoms were followed on the next day by drowsiness and pain in the abdomen. The voice became very weak. On the day before admission, the patient was "tender on being touched anywhere." He had been confined to bed since the onset of symptoms, but had seemed to his parents to become progressively weaker and to behave in a "queer" manner.

Physical examination of the patient on admission showed extreme apathy and stupor. The temperature was 101 F., the pulse 120. There was a frequent, weak and ineffective cough. Respirations were 40 per minute and diaphragmatic. There was no cyanosis at this time. The neck was stiff, but Kernig's sign was not present. There was weakness of the extremities on both sides; more marked on the right. There appeared to be no involvement of the cranial nerves. The patient was considered too ill to undergo a lumbar puncture. The diagnosis was acute poliomyelitis with respiratory paralysis.

Six hours after admission the patient became cyanotic. Oxygen was administered through a nasal catheter, and 0.03 gm. of caffein, and 0.0003 gm. of atropin, were given hypodermically. At this time there was absence of intercostal breathing and no visible motion of the diaphragm on the right side. With each inspiration the alae nasae moved and the epigastrium bulged slightly on the left. The palate was not paralyzed, but the saliva was not swallowed and there was almost continuous drooling. Intravenous glucose, 200 c.c. of a 20 per cent. solution, was given slowly; there was no appreciable effect.

Ten hours after admission the cyanosis had increased and the patient seemed to be dying. Those who observed the boy felt that he would probably not live longer than two hours. Almost the only muscular activity displayed was in the movements of the eyes. It was then decided, as a heroic measure, to try hypertonic saline solution intravenously. Accordingly, with the consent of the

parents, 40 c.c. of a 30 per cent. sodium chlorid solution was injected slowly into the right femoral vein. The immediate reactions were pallor, a rapid, weak pulse, and a temporary cessation of respirations.[4] After a few moments respirations began slowly and continued steadily, but were still performed entirely by the left half of the diaphragm. One-half hour later the patient asked for water which was allowed in small sips.

Nine hours after treatment, the following note was made: The patient's color was good, his voice was stronger, the entire (?) diaphragm was functioning; the abdominal, creamasteric and patellar reflexes were obtained on both sides; the improvement in the general condition was quite striking; the patient was very thirsty. Oxygen was discontinued at this time.

Twenty-four hours after treatment, the patient was markedly improved; the physical findings were much the same as given in the preceding paragraph.

Forty-three hours after treatment, the patient showed Kernig's sign and the neck was stiff. The temperature rose to 103 F. and there was slight cyanosis; oxygen was resumed for short time. There was gradual amelioration of the symptoms within the next twenty-four hours.

Six days after treatment, the patient was markedly improved and breathed with both sides of the diaphragm.

The boy was discharged forty-seven days after admission. Physical examination showed paralysis of the recti abdominis, the intercostal muscles on both sides and the tibialis anticus on the right. There was marked weakness of the right deltoid, triceps and biceps.

The patient continued to improve gradually and has passed satisfactorily through a moderately severe attack of whooping cough. The intercostals remain paralyzed.

COMMENT

This case has been reported with the object of putting on record the treatment employed. This is the only patient whom we have thus treated, but it seems highly probable that the life of this boy was saved by the therapeutic measures employed. No one who saw the child just before treatment believed it possible for him to live. We have no basis for belief in the efficacy of the treatment other than that obtained from clinical observation and comparisons. Of course, the administration of saline solution and the child's recovery may have been simply coincident and in no way related as cause and effect. However, everyone who saw the patient throughout the period of critical illness was sufficiently impressed by the sudden reversal in his condition after intravenous therapy to believe that in a similar case similar treatment should be tried. We are, of course, in no position to define the optimum concentration or dosage of saline solution.

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4. Dr. Amoss has been kind enough to make the following valuable criticism of the treatment in the case reported: "Forty cubic centimeters of a 30 per cent. sodium chlorid solution was given and there was marked reaction afterward. The depressant effect of sodium might possibly be the reason. Attention might be called to the fact that this depressor action might be prevented, if a sufficient amount of calcium was added to antagonize the sodium."

INSULIN IN MALNUTRITION *

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AND
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During the last two years, the use of insulin in various degrees of malnutrition in infancy has been studied with increasing interest and with varying results. Viewing their own work with a critical eye, all authors are not agreed as to the value of this procedure.

REVIEW OF THE LITERATURE

Pitfield [1] was the first to work with insulin in infants. He tried injections in two babies, aged 4 and 5 months respectively, who were suffering from malnutrition. In each case the child was receiving a formula with an energy quotient of 80 calories per pound, without gain. Following minute doses of insulin with every bottle, there was a gain in weight, with better digestion and great improvement in the color and general condition of the child.

Later, Marriott [2] reported uniformly successful results in malnourished infants by using injections of a solution of glucose, to which insulin had been added in order to bring about better utilization of the sugar with a resultant gain in weight.

In a number of cases of severe athrepsia, Marriott felt that, except for this injection, the death of the infant would undoubtedly have occurred within a few days or hours. It has been possible for us to verify this impression in several of our cases of acute intoxication, described later in this paper.

Following Marriott's work, Barbour [3] reported beneficial results in cases of nondiabetic, malnourished children from the use of insulin. The dose was injected subcutaneously, all children under 2 years receiving 3 units three times daily, twenty minutes before meals; those over 2 years of age receiving 5 units thrice daily. The insulin was pushed to the limit of the individual capacity in order to obtain maximum results. Administration of the remedy was continued as directed in the foregoing until a reaction appeared, indicated by a sudden rise in

* Received for publication, Oct. 6, 1925.
* From the Infantorium and Heckscher Foundation.

1. Pitfield, R. L.: New York M. J. **118**:217 (Aug. 18) 1923.
2. Marriott, W. McK.: The Food Requirements of Malnourished Infants, J. A. M. A. **83**:600 (Aug. 23) 1924.
3. Barbour, O.: The Use of Insulin in Undernourished, Nondiabetic Children, Arch. Pediat. **41**:707 (Oct.) 1924.

temperature, anorexia, nausea and vomiting. The preparation was stopped for twenty-four hours, then was given twice daily until a second reaction occurred; it was stopped again for twenty-four hours and resumed once daily until a third reaction resulted, after which the insulin was discontinued. Of forty patients thus treated, thirty-eight showed definite improvement in their condition.

Tisdall and his co-workers,[4] on the other hand, having studied the effect of insulin on blood sugar concentration, have recently expressed a different opinion. The facts that blood sugar concentration varies greatly under the influence of insulin, and that certain infants have a very marked hypoglycemia without showing a hypoglycemic reaction, have led these authors to feel that a certain element of danger attends the use of insulin. In their work, the insulin was used intravenously with 20 per cent. glucose solution as well as subcutaneously with 15 per cent. glucose, and in conjunction with the feeding. Tisdall concludes that "no positive evidence has been obtained that insulin per se, when administered with carbohydrate to malnourished infants, produces any beneficial results."

Since the ultimate significance of insulin in various forms of malnutrition can only be determined by an accumulation of results, we wish to present our series of cases and the conclusions we have been able to draw.

METHOD OF PROCEDURE

Insulin [5] may be administered in a number of ways, as follows:

1. In combination with a solution of glucose.

(*a*) Intravenous or intrasinus injections of from ⅓ to ½ ounce (from 9 to 14 gm.) of 20 per cent. glucose per pound of body weight, to which have been added 15 units of insulin per hundred cubic centimeters of solution (Marriott).

(*b*) Intraperitoneal injections of from to 2 to 3 ounces (from 56 to 85 gm.) of 20 per cent. glucose solution, containing from 10 to 15 units of insulin.

(*c*) Subcutaneous injections of from 2 to 3 ounces of a 15 per cent. glucose solution with 10 units of insulin by hypodermoclysis.

2. In conjunction with feedings.

(*a*) From 1 to 3 units subcutaneously twice to three times daily, twenty minutes before meals, until some reaction is evident.

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4. Tisdall, F. F.; Brown, A.; Drake, T. G. H., and Cody, M. G.: Insulin in the Treatment of Malnourished Infants, Am. J. Dis. Child. **30**:10 (Aug.) 1925.

5. The preparations of insulin used in this work were insulin-Lilly and insulin-Squibb.

(*b*) From 1 to 3 units intracutaneously, once daily, on the basis of work done by Müller,[6] who explained that insulin thus given works at once by stimulating the liver glycogen forming function, through nerve stimuli passing over the parasympathetic nerve routes. This causes a quick reduction of blood sugar. It is further explained that insulin administered intracutaneously is more slowly absorbed than by other routes, which accounts for a prolonged action of the dose, when injected into the skin. Direct action of the insulin on the blood only occurs by secondary absorption from the wheal formed at the site of injection.

Administration of Insulin

Case	Date	Age, Weeks	Weight at Beginning of Treatment		Progress Before Insulin	Progress After Insulin	Remarks
			Lb.	Oz.			
1	3/11/25	10	6	9	2 weeks, lost 1 lb. 4 oz.	12 days, gained 1 lb. 8 oz.	Atrophy, toxic; successful
2	8/29/24	22	10	..	?	4 weeks, gained 1 lb. 14 oz.	Atrophy, toxic; successful
3	4/25/25	34	13	12	2 weeks, lost 11 oz.	2 weeks, stationary	Atrophy, toxic; improved
4	7/26/25	7	5	14	2½ weeks, lost 5 oz.	2½ weeks, gained 2 oz.	Toxic; improved
5	3/17/25	5	6	5	2 weeks, lost 1 lb. 7 oz.	2 weeks, lost 1 lb. 1 oz.	Toxic; expired
6	4/ 5/25	9	6	8	15 days, gained 1 oz.	9 days, gained 12 oz.	Atrophic; successful
7	4/ 4/25	4	4	7	8 days, stationary	5 days, gained 1 oz.	Removed; indifferent
8	7/27/25	20	7	4	2 weeks, stationary	2 weeks, gained 12 oz.	Acute atrophy; successful
9	4/ 3/25	5	6	6½	5 days, lost 14½ oz.	10 days, gained 14½ oz.	Acute atrophy; successful
10	8/19/25	3	4	15	12 days, gained 1 oz.	20 days, gained 1 lb. 3 oz.	Acute atrophy; successful
11	6/ 8/25	56	19	13½	2 weeks, lost 8 oz.	3 weeks, gained 1 lb. 4 oz.	Successful
12	11/15/24	5	5	11	2 weeks, lost 1 oz.	8 days, gained 12 oz.	Dystrophic; successful
13	11/15/25	3	6	5	16 days, gained 3 oz.	11 days, gained 11 oz.	Successful
14	3/18/25	48	15	10	2 weeks, stationary	13 days, gained 13 oz.	Dystrophic; successful
15	2/ 5/25	20	8	13	3 weeks, lost 1 oz.	3 weeks, gained 1 lb. 5½ oz.	Dystrophic; successful
16	4/ 2/25	22	9	8	12 days, gained 5 oz.	7 days, gained 13 oz.	Dystrophic; successful
17	4/ 8/25	22	12	11	19 days, gained 1 oz.	6 days, gained 1 lb. 1 oz.	Successful
18	4/ 3/25	8	3	..	10 days, stationary	7 days, gained 4 oz.	Hypotrophic; indifferent
19	3/29/25	10	8	6	8 days, stationary	11 days, gained 10 oz.	Confusing
20	3/29/25	7	5	13¾	9 days, gained 1¾ oz.	7 days, gained 4 oz.	Indifferent
21	4/ 2/25	5	7	9	7 days, lost 1 lb. 3 oz.	7 days, gained 1 lb.	Successful
22	10/16/24	12	10	14	16 days, gained 9 oz.	16 days, gained 12 oz.	Indifferent
23	3/30/25	10	6	4¾	12 days, gained 8 oz.	15 days, gained 19¾ oz.	Confusing
24	3/29/25	3	5	10½	12 days, lost 5½ oz.	12 days, gained 1 lb. 2½ oz.	Confusing
25	7/28/25	10	6	12½	3 weeks, lost 4¾ oz.	3 weeks, gained 15 oz.	Confusing
26	6/28/25	11	8	13	14 days, gained 6 oz.	14 days, gained 8½ oz.	Dystrophic; indifferent
27	7/28/25	10	7	13	25 days, gained 3 oz.	20 days, gained 13 oz.	Dystrophic; successful

6. Müller, E. F.; Wiener, H. E., and Wiener, R. von E.: Proc. Soc. Biol. & Med. (April) 1925; München. med. Wchnschr. **72**:1061, 1925.

INDICATIONS FOR USE

In our choice of methods enumerated in the foregoing, three types of cases are considered, the variations are made to suit the individual need.

1. A state of atrophy with acute intoxication, in which life is in danger and the urgency of remedial measures demands the quickest possible absorption for an immediate effect. In such cases we have resorted to Marriott's method of injecting a 20 per cent. solution of glucose with insulin intravenously. In our work, we injected into the longitudinal sinus through the anterior fontanel. With a careful technic we have never seen disastrous results from this procedure. Of five patients with acute intoxication thus treated in our series, four were treated successfully and one expired. The individual results are discussed in a later description.

2. Cases of atrophy in which decomposition and acute intoxication have not yet set in. In such infants, we have limited our efforts to intraperitoneal or subcutaneous injections of insulin and glucose.

3. Dystrophic babies, who are below normal, with a stationary weight, or who gain irregularly with great fluctuations and who, at the end of many weeks, show no progress at all. Such children are generally pale, apathetic and indifferent to food. In a number of patients of this type we have seen excellent improvement, when insulin was given subcutaneously or intracutaneously in conjunction with the unchanged formula.

DESCRIPTION OF CASES

In the cases here described, we endeavored to eliminate as many factors as possible, which might lead to confusion in interpreting the final results obtained. Important among these is the diet. Insulin was not used until an appropriate formula had been given the opportunity to work. If this failed to help, the insulin was then tried and the diet was kept constant throughout the period of trial, so that in our work we could not have difficulty in deciding whether a successful result was due to insulin or to a change in formula. The latter was always kept constant.

CASE 1.—A. L., aged 10 weeks, who weighed 6 pounds, 9 ounces (2.9 kg.), was a typical example of acute atrophy with intoxication. The child became severely ill, with an elevation of temperature to 104 F., and rapidly lost weight. Acute intoxication followed. Albumin milk and dextrimaltose were used in increasing amounts up to 3 ounces (85 gm.) of the milk, and 2½ teaspoons of the dextrimaltose every three hours. There was a slight improvement in weight, but the child remained toxic. Twelve hours after an intrasinus injection of 60 c.c. of 20 per cent. glucose and 10 units of insulin, the toxicity abated and improvement was rapid. Within twelve days there was a gain of 1½ pounds (0.6 kg.).

CASE 2.—J. B., aged 5 months, weighing 10 pounds (4.5 kg.), who was severely marantic, was admitted in a state of acute intoxication and apparently dying. No hope for recovery was offered. It was decided, however, to use glucose and insulin intrasinusly. Fifteen units of insulin were combined with 60 c.c. of a 20 per cent. glucose solution, and were given daily for three days. Four hours after the first injection the patient was distinctly better. The toxic stare and the rapid, labored respiration had disappeared. Actual gain in weight did not begin until two weeks later. The significant fact here was the sudden and marked disappearance of the acute symptoms of intoxication.

CASE 3.—H. K., aged 6 months, weighed 14 pounds, 7 ounces (6.6 kg.). This child was also toxic. Five units of insulin were combined with 60 c.c. of 20 per cent. glucose and were given intraperitoneally. Here again a marked decrease in toxicity was evident, giving new hope for recovery, which ultimately followed.

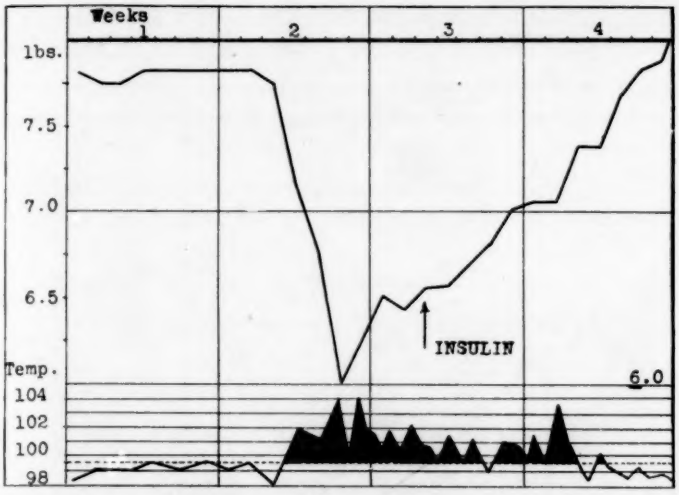

Chart 1 (Case 1).—Acute intestinal indigestion with atrophy and severe intoxication.

CASE 4.—J. A., aged 7 weeks, who weighed 5 pounds, 4 ounces (2.4 kg.), had atrophy with marked dehydration and acute intoxication. The temperature was 103 F. The stools were loose and green, with much mucus. As in a former patient (Case 2), recovery seemed impossible and death imminent until insulin was used. Ten units were combined with 2 ounces (56 gm.) of 20 per cent. glucose, and were given through the anterior fontanel on three successive days. There was a further loss in weight of 9 ounces (255 gm.) followed by a rapid gain. At the time of writing (two months later), the child had completely recovered and was developing rapidly on the original diet of breast milk, alternated with albumin milk feedings, which were begun at the time of the illness.

CASE 5.—J. H., aged 5 weeks, who weighed 6 pounds, 4 ounces (2.9 kg.), was marantic, with acute intoxication. This patient, similar to J. A. (Case 4), received glucose and insulin, but did not recover.

CASE 6.—R. d. A., aged 9 weeks, who weighed 6 pounds, 8 ounces (3 kg.), and was malnuorished and atrophic, had been doing rather poorly for several weeks on a formula amounting to 85 calories per pound of body weight. This was a case of simple atrophy. A sudden loss of weight occurred, with a rise in

temperature to 103.5 F. The stools were loose and frequent. Without changing the formula, it was decided to try a dose of 3 units of insulin with 60 c.c. of a 15 per cent. glucose solution, subcutaneously. The loss in weight was checked and a rapid gain with consequent improvement justified the experiment.

CASE 7.—R. S., aged 4 weeks, weighed 4 pounds, 7 ounces (2 kg.). This baby was premature, weighing 4 pounds, 13 ounces (2.1 kg.), at birth. After a slow, but progressive loss of weight, we used three subcutaneous doses of 1 unit of insulin and 30 c.c. of 15 per cent. glucose. The improvement was slight. The child was removed before larger doses could be tried, and the result was considered indifferent.

CASE 8.—F. T., aged 20 weeks, who weighed 7 pounds, 4 ounces (3.3 kg.), was severely atrophic. Following a subcutaneous injection of physiologic sodium chlorid, the patient developed a circular ulcer, about 1½ inches in diameter, in the left lower quadrant of the abdominal skin. There was a complete sloughing away of tissue down to the muscle. The extremely poor nutrition of the child and the size of the ulcer led to a bad prognosis from the consultant surgeon. The infant was placed on breast milk, with additions

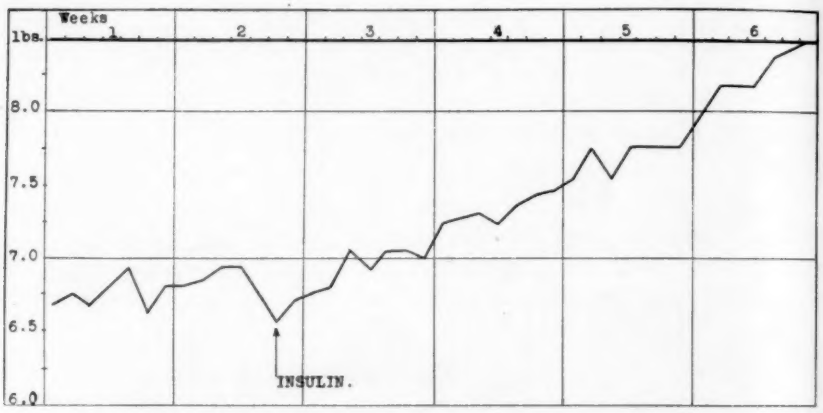

Chart 2 (Case 6).—A case of simple atrophy.

of dextrimaltose. This was tolerated poorly at first. Hypodermically, one unit of insulin was given daily for four days. Improvement in the general condition with sudden and progressive gain in weight began; the appetite was better and the vomiting ceased. The ulcer began to heal rapidly, and within a month a new scar tissue had grown completely over the wound. This successful result was far beyond our hopes.

CASE 9.—V. F., aged 5 weeks, who weighed 6 pounds, 6½ ounces (2.8 kg.), was acutely ill, with an elevation of temperature to 102 F., and frequent, watery, green stools with much mucus. Rapid dehydration followed, with a loss of 1 pound, 2 ounces (0.6 kg.) in five days. The child began to appear toxic. Insulin was given subcutaneously in 2 unit doses, four times in ten days. There was an immediate response to this therapy with a resultant gain of 14½ ounces (403.9 gm.) in ten days. Albumin milk with sucrose was started when the severe loss in weight set in, and was used throughout the illness in unchanged amounts.

CASE 10.—J. I., aged 3 weeks, who weighed 4 pounds, 15 ounces (2.2 kg.), was one month premature, the birth weight being 4 pounds, 2 ounces. The formula was breast milk, 2 ounces (56 gm.); dextrimaltose, 1 teaspoon, and powdered protein milk, 1 teaspoonful every three hours. Twelve days after

admission, the child had gained only 1 ounce (28 gm.). A sudden elevation of temperature to 102 F. developed; the baby became extremely pale, the pulse weak and the breathing dyspneic. It was feared the child would die. Sixty cubic centimeters of a 15 per cent. glucose solution was given intraperitoneally, and 10 units of insulin were given subcutaneously. From this point improvement was rapid. The temperature fell to normal on the same day, and a steady and rapid progress followed, so that twenty days later there was a gain of 1 pound, 3 ounces, with a corresponding improvement in color, nutrition and general development. This child was one of twins, similar in weight on admission, and who were on the identical formula. The comparison of progress is interesting. The second child suffered from no acute illness and received no insulin. At the time of writing the latter child is small, pale, thin, and not thriving nearly so well as the patient in question.

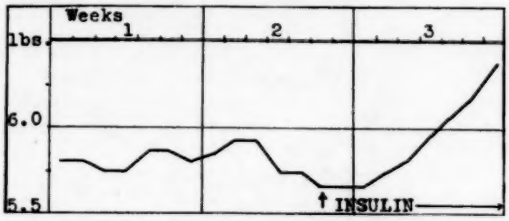

Chart 3 (Case 12).—The effect of insulin given subcutaneously, thrice daily for eight days.

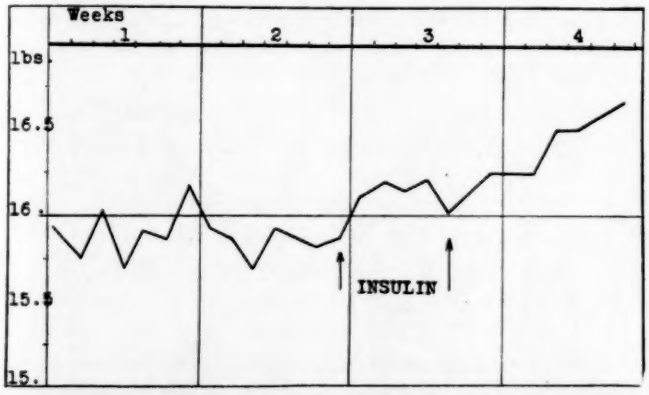

Chart 4 (Case 14).—Result after 2 units of insulin subcutaneously, thrice daily, fifteen minutes before meals, for six days.

Dystrophy.—Most of the patients in this series were of a dystrophic nature, who had either been much neglected in the early months of life and were, in consequence, seriously malnourished and slow in gaining, or were those with a constitutional hypotrophy at birth, who remained stationary in weight with but slow and irregular development. Of these, only the most significant cases will be discussed.

Case 11.—H. G., aged 13 months, weighed 19 pounds, 13½ ounces (8.9 kg.). For many days this child throve poorly, gaining irregularly and losing frequently, so that two weeks after admission 8 ounces (226 gm.) had been lost. The

baby was pale but happy, and was quite indifferent to food. Insulin therapy suggested itself, and was given in two doses of 2 units intracutaneously into the skin of the forearms, on two successive days. The appearance of the wheal and the remaining area of bronze pigmentation reminded one vividly of the Schick test. For a week after the administration of insulin, there was little improvement, except for a check in the progressive loss of weight. Then there appeared a gradual gain, coincident with a perceptible improvement in the child's appetite and color of the skin. In three weeks from the time of treatment, 1 pound, 4 ounces (0.7 kg.) had been gained.

CASE 12.—W. P., aged 5 weeks, whose weight was 5 pounds, 11 ounces (2.6 kg.), weighed 5 pounds, 5½ ounces at birth. For two weeks previous to the insulin therapy this child had lost 1 ounce. Insulin was then given in doses

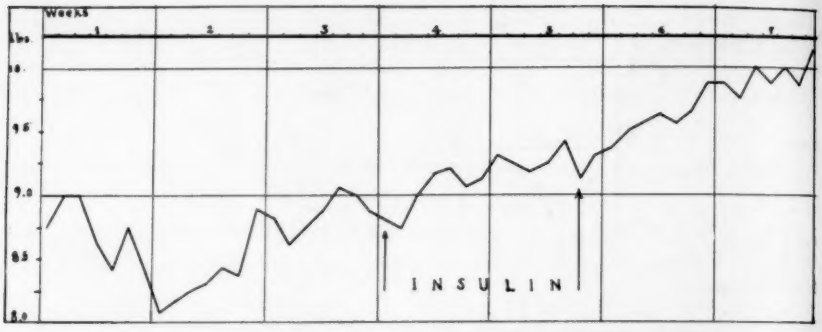

Chart 5 (Case 15).—The effect of 1 unit of insulin subcutaneously for thirteen days on a fluctuating weight curve, after three weeks without progress.

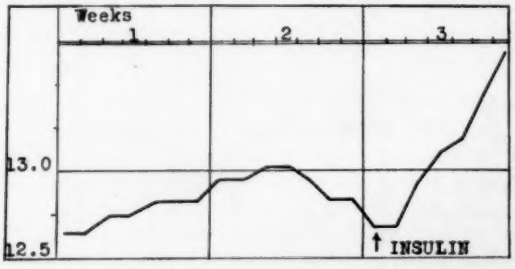

Chart 6 (Case 17).—The effect of one dose of 3 units of insulin.

of 2 units, three times daily, fifteen minutes before meals, for eight days, during which period there was a gain of 12 ounces, with marked general improvement. The formula, amounting to 92 calories per pound of body weight, was not changed for a period of two weeks before or after the insulin treatment began. All other routine was kept as constant as possible.

CASE 13.—S. W., at the age of 3 weeks weighed 6 pounds, 5 ounces (2.8 kg.). Having gained only 3 ounces (85 gm.) in the sixteen days following admission, insulin was given subcutaneously in doses of 1 unit for eleven days. During this period a gain of 11 ounces (311 gm.) was recorded.

CASE 14.—J. B., aged 11 months, who weighed 15 pounds, 10 ounces (7.1 kg.), was severely dystrophic. After two weeks without gain, insulin was given in doses of 2 units, subcutaneously, thrice daily before meals. The improvement was prompt. In thirteen days there was a gain of 13 ounces (368 gm.). This

was checked by the development of a sudden attack of double acute otitis media, with a rise in temperature and a corresponding loss in weight. Following paracentesis, the child quickly recovered.

CASE 15.—A. A., aged 20 weeks, who weighed 8 pounds, 13 ounces (3.9 kg.), had severe malnutrition with irregular fluctuations of weight over a long period of time. The first two weeks in Figure 5 illustrate exactly what had been going on for six weeks previously.

One unit of insulin was administered subcutaneously, twice daily, fifteen minutes before meals, for thirteen days, resulting in a tendency to gain steadily with only occasional and unimportant remissions.

CASE 16.—G. F., aged 22 weeks, who weighed 9 pounds, 8 ounces (4.3 kg.), was severely dystrophic, with a period of stationary weight for one month following admission. Seven days after a hypodermic dose of 2 units of insulin, the patient had gained 13 ounces (368 gm.), which was a good result.

CASE 17.—M. F., aged 22 weeks, weighed 12 pounds, 11 ounces (5.7 kg.). This child was also dystrophic and was making poor progress. For fourteen days prior to the administration of insulin, a gain of but 1 ounce (28 gm.) had been recorded. Six days after an injection of 3 units of insulin, without change of formula, there was a gain of 1 pound, 1 ounce (0.7 kg.).

COMMENT

In this work on the value of insulin in various types of malnourished infants, a number of interesting observations should be mentioned. Our results have not been sensational. We have had cases of acute intoxication, in which we have felt that insulin alone has proved the life-saving factor. In other less acute cases there has been definite improvement in nutrition and in appearance, which we can attribute to the administration of insulin only. In a number of dystrophic infants with stationary weight, a result following insulin was noticed only after one or two weeks had elapsed when a gradual improvement was observed. There having been no changes in diet, we feel that a number of these results were in some way associated with the use of the insulin principle. In some cases, on the other hand, in which we hoped for favorable results, insulin has proved entirely without effect and was discontinued after a reasonable trial.

We have discovered no ill effects from individual, small doses of insulin, nor even from large doses combined with glucose in solution. But what appears to be a cumulative effect has beeen observed. If a child be given insulin regularly, twice or three times a day, in doses of from 1 to 5 units, a reaction follows after a number of days. This consists of a rise in temperature, which may be slight, or as high as 102 F., a loss of appetite with a decrease in weight and general indisposition. Discontinuing insulin has been sufficient to remedy this condition.

We have already described the types of cases in which insulin has been tried. In our work it has justified its use as a last resort in most cases of severe atrophy with intoxication. Not all infants with dystrophic tendencies, however, are suitable for this therapy. We have

often been mistaken in our judgment of appropriate cases for insulin. In general, however, the clinical appearance of a child, who may be expected to improve under the treatment in question, is that of an infant with a moderate degree of anemia, somewhat apathetic to its environment and with no interest in its food. This type of child is much undernourished, often being several pounds underweight, and one whose weight curve either fluctuates without ultimate gain, or remains stationary without gain or loss over a period of weeks.

Realizing, then, the limitations of this form of treatment and that the use of insulin must be undertaken with discretion, and keeping in mind what others have already written on this subject, it is still our impression, after reviewing our experiences with the preparation, that, in types of cases discussed, insulin may be used with a reasonable hope of success, when other suggestions in diet and management have failed.

SUMMARY

1. This paper is devoted to a report of the results obtained in twenty-seven malnourished infants, who were given insulin. Of these, seventeen results (63 per cent. of our cases) were distinctly successful, with marked gain in weight and improved nutrition. Five cases were indifferent, showing no change during or after treatment. Four cases were confusing, so far as a change of formula was necessary during the period of trial. One child died in a state of acute intoxication, despite the persistent use of insulin intravenously.

2. Three types of malnutrition were treated in the following manner: In cases of acute atrophy with intoxication, insulin was given in combination with a 20 per cent. solution of glucose, intravenously, through the anterior fontanel. Of five cases thus treated, four recovered. In atrophy without intoxication, insulin was administered with 15 per cent. glucose, intraperitoneally or subcutaneously. In dystrophy, insulin was used subcutaneously or intracutaneously in conjunction with the feedings.

3. In those cases reported as successful, there were no changes in diet or in management, other than the use of insulin combined with glucose, to which improvement could have been attributed.

4. No ill effects from individual doses of insulin were observed.

5. Insulin given in repeated, small doses seems to have a cumulative effect, which culminates in a rise in temperature, anorexia and loss of weight.

CONCLUSION

Insulin, if administered in properly chosen cases of malnutrition in infancy, has been an effective, though not absolute, remedy in our hands, and deserves a trial when all other methods of feeding and management have failed.

PREVALENCE AND PREVENTION OF ACUTE RESPIRATORY DISEASES IN CHILDREN UNDER FIVE YEARS OF AGE

CHICAGO PNEUMONIA COMMISSION, REPORT NO. 2*

HUGH O. JONES, M.D.
Chief of Child Hygiene, Department of Health Bureau
CHICAGO

Early in the investigations of the Chicago Pneumonia Commission,[1] it was found that the death rates from the acute respiratory diseases were exceedingly high in children under 5 years of age, and that, therefore, the occurrence of the diseases at this age period deserved special consideration.

The annual death rates from the acute respiratory diseases in Chicago in children under 5 years of age (from 1905 to 1924), per 100,000 of population at this age period are shown in Chart 1. This chart also shows the death rates from the acute respiratory diseases at all ages, per 100,000 population. The term, acute respiratory diseases as used in this report, includes pneumonia (all forms), acute bronchitis and influenza.

An analysis of these rates shows the following relationship of the deaths from the acute respiratory diseases in children under 5 years of age to the total death rate from acute respiratory diseases.

The number of deaths from the acute respiratory diseases occurring annually in children under 5 years of age now exceeds those due to the acute diarrheal diseases. This excess death rate from the acute respiratory diseases at this age period occurred for the first time in 1918, and has continued each year since 1921.

AGE DISTRIBUTION

The age distribution of deaths from the acute respiratory diseases in children under 5 years of age, in Chicago, for the period from Oct. 1, 1923, to Sept. 30, 1924, is shown in Table 2, by three month periods, together with the death rate for each age period, based on the Chicago Health Department's estimates of population at these age periods.

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* Received for publication, Dec. 7, 1925.

* The members of the commission include: Dr. Herman N. Bundesen, chairman; Dr. C. C. Pierce, United States Public Health Service; Dr. Isaac D. Rawlings, director of public health of the state of Illinois; Dr. W. A. Evans, health editor of the Chicago Tribune; Dr. Edwin O. Jordan, of the University of Chicago; Dr. Carey J. Vaux, director of department of public health, Pittsburgh; Dr. J. C. Geiger, assistant commissioner of health of Chicago, and Dr. G. Koehler, assistant commissioner of health of Chicago, secretary.

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It will be noted that the death rate is highest in the 1 month to 1 year group, being 1,405 per 100,000, as compared with 190.4 in the age group 4 to 31 days, and 172.6 per 100,000 in the group 1 to 4 years.

The table shows strikingly the reduction in the acute respiratory disease death rate at the end of the 5 year age period, the rates for the two succeeding 5 year periods averaging approximately 18.5 per 100,000 for each period.

TABLE 1.—*Acute Respiratory Disease Death Rates Per 100,000 Population All Ages and Per 100,000 Population Under 5*

Period	All Ages	Under 5	Per Cent of All Deaths Under 5 Years
1915–1924	206.6	710.7	34.7
1905–1914	225.1	986.7	44.7

TABLE 2.—*Age Distribution Decedents From Acute Respiratory Diseases Under 5 Years of Age, Also Age Groups 5 to 9 and 10 to 19 Years, October, 1923, to September, 1924*

Age	1923 Oct.-Dec.	1924 Jan.-March	1924 April-June	1924 July-Sept.	1923-24 Oct.-Sept.	Death Rate per 100,000 of Age Group
4 to 7 days	..	...	...	..	...	.....
8 to 31 days	5	2	2	0	9	190.4
1 to 5 months	81	163	112	48	404	
6 months to 1 year	47	121	106	44	318	1,405
1 year to 4 years	84	183	108	47	422	172.6
5 to 9 years	15	15	16	5	53	18.7
10 to 19 years	18	26	27	14	85	18.3

TABLE 3.—*Age Distribution Cases of Acute Respiratory Disease Under 5 Years of Age, Also Age Groups 5 to 9 and 10 to 19 Years— January to September, 1924, Inclusive*

Age	Jan.-March	April-June	July-Sept.	Jan.-Sept.	Per Cent of Total Cases
4 to 6 days	4	3	0	7	0.1
1 to 4 weeks	21	10	4	35	0.5
1 to 5 months	206	94	14	314	4.8
6 to 11 months	234	164	21	419	6.3
1 to 4 years	744	394	96	1,234	18.7
5 to 9 years	276	221	50	547	8.3
10 to 19 years	235	172	47	454	6.9

From Jan. 1, 1924, to Sept. 30, 1924, 6,601 cases of pneumonia were especially investigated by the Pneumonia Commission. Of these, 2,009, or 30.4 per cent., occurred in children under 5 years of age. The age distribution of this latter group is shown in Table 3.

SEASONAL VARIATIONS

Table 2 shows the deaths by three month periods in children in the various age groups under 5. The weekly death rates from the acute respiratory diseases among children under 5 years of age in Chicago

(October, 1923, to September, 1924), as well as the rates for the 5 to 49 year and 50 year and over age groups, are shown in Chart 2.

This chart shows that the rise in the rate of the 50 and over group starts about October 19; the rise in the rate of the under 5 group starts about November 23, the great rise starting about January 1. In the 50 and over group the great rise begins about March 21, while in the 5 to 49 group the rise starts about November 1 and peaks about March 21.

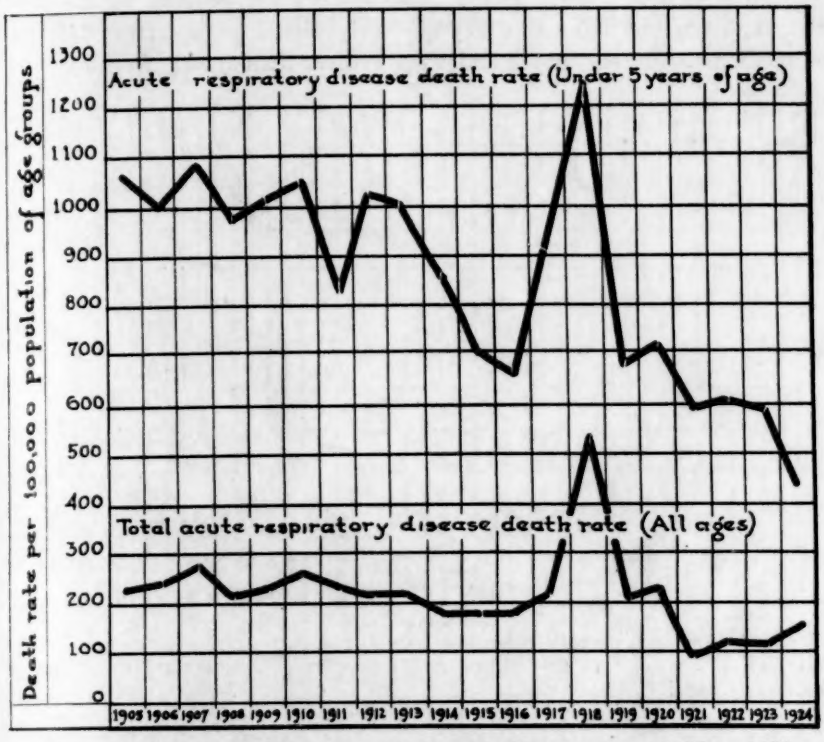

Chart 1.—Death rate from acute respiratory diseases from 1905 to 1924.

The greatest seasonal fluctuation is in the under 5 group, the next in the 50 and over; in comparison, the seasonal fluctuation in the 5 to 49 group is slight.

COLOR

Death rates of white and colored children and those of other races combined, from acute respiratory diseases, per 100,000 population of the age group under discussion, are shown in Chart 3.

It will be noted that the death rate among colored children is approximately ten times as high as that of white children, and that the acute

respiratory diseases are relatively more frequent causes of death among the colored.

The group marked "others" is small and should, therefore, be given but little weight.

SEX

The sex of decedents from the acute respiratory diseases is shown in Table 4, for quarterly periods. It is interesting to note that there were 15 per cent. more deaths among males than among females, while the census figures show that the males exceed the females by 2.3 per cent. at this age period. In every quarterly period, except from July to September, the deaths among males are greater than among females.

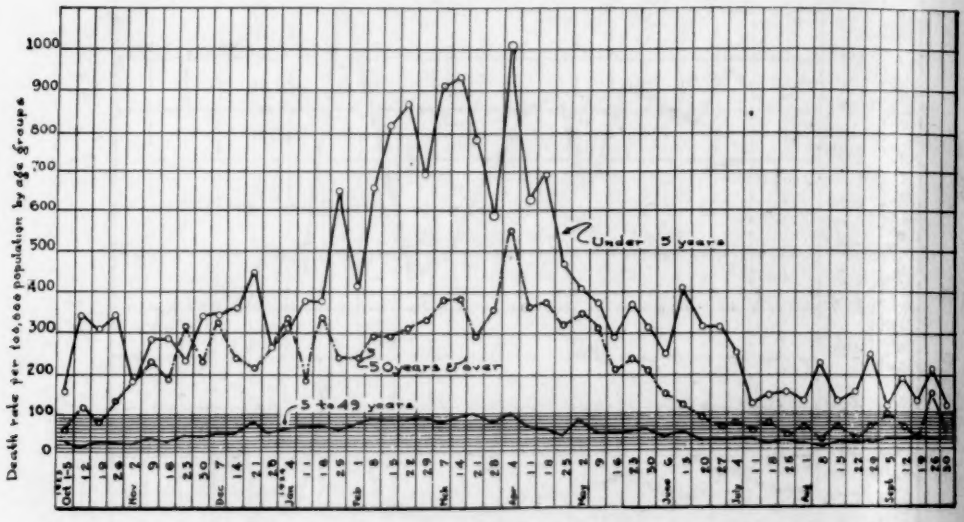

Chart 2.—Weekly death rates per 100,000 population from acute respiratory diseases for age groups as follows, under 5 years of age, from 5 to 49 and 50 years and over.

TABLE 4.—*Sex of Decedents Under 5 Years of Age From Acute Respiratory Diseases—October, 1923, to September, 1924*

Sex	1923 Oct.-Dec.	1924 Jan.-March	1924 April-June	1924 July-Sept.	Total Oct.-Sept.
Male	126	278	190	69	663
Female	91	191	138	70	490

GEOGRAPHICAL DISTRIBUTION

The geographical distribution of the deaths from acute respiratory diseases, all ages, is shown in Chart 4. The wards having a death rate above the average for the entire city are shaded. The wards showing a death rate 100 per cent. above the average have a large colored population.

ANATOMIC CLASSIFICATION

The anatomic types of acute respiratory diseases, as classified by the commission, occurring in age periods under 5, are shown in Table 5, together with the anatomic types occurring at all ages. It will be noted that bronchopneumonia caused 61.6 per cent. of the deaths from the acute respiratory diseases in children under 5, as contrasted with only 33 per cent. at all ages.

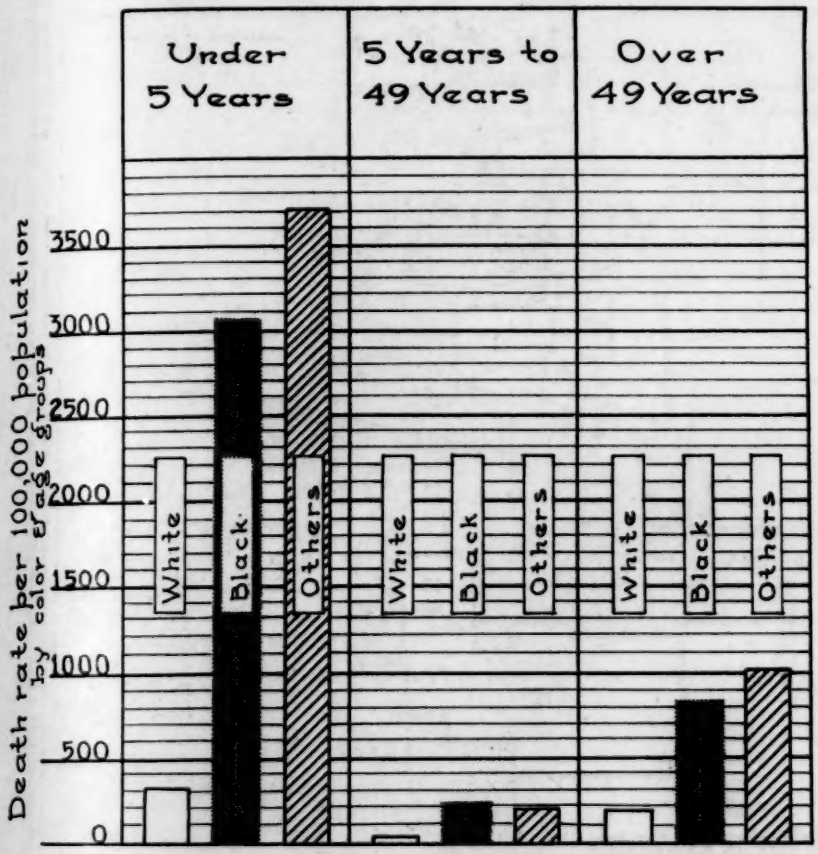

Chart 3.—Color of decedents by age periods and death rates per 100,000 population from acute respiratory diseases. October, 1913, to September, 1924.

The classifications used in the table are based on the death certificates. The commission does not consider that the anatomic diagnosis is altogether dependable.

RECOMMENDATIONS

The commission recommends the following measures for the reduction of the acute respiratory disease rate at this age period:

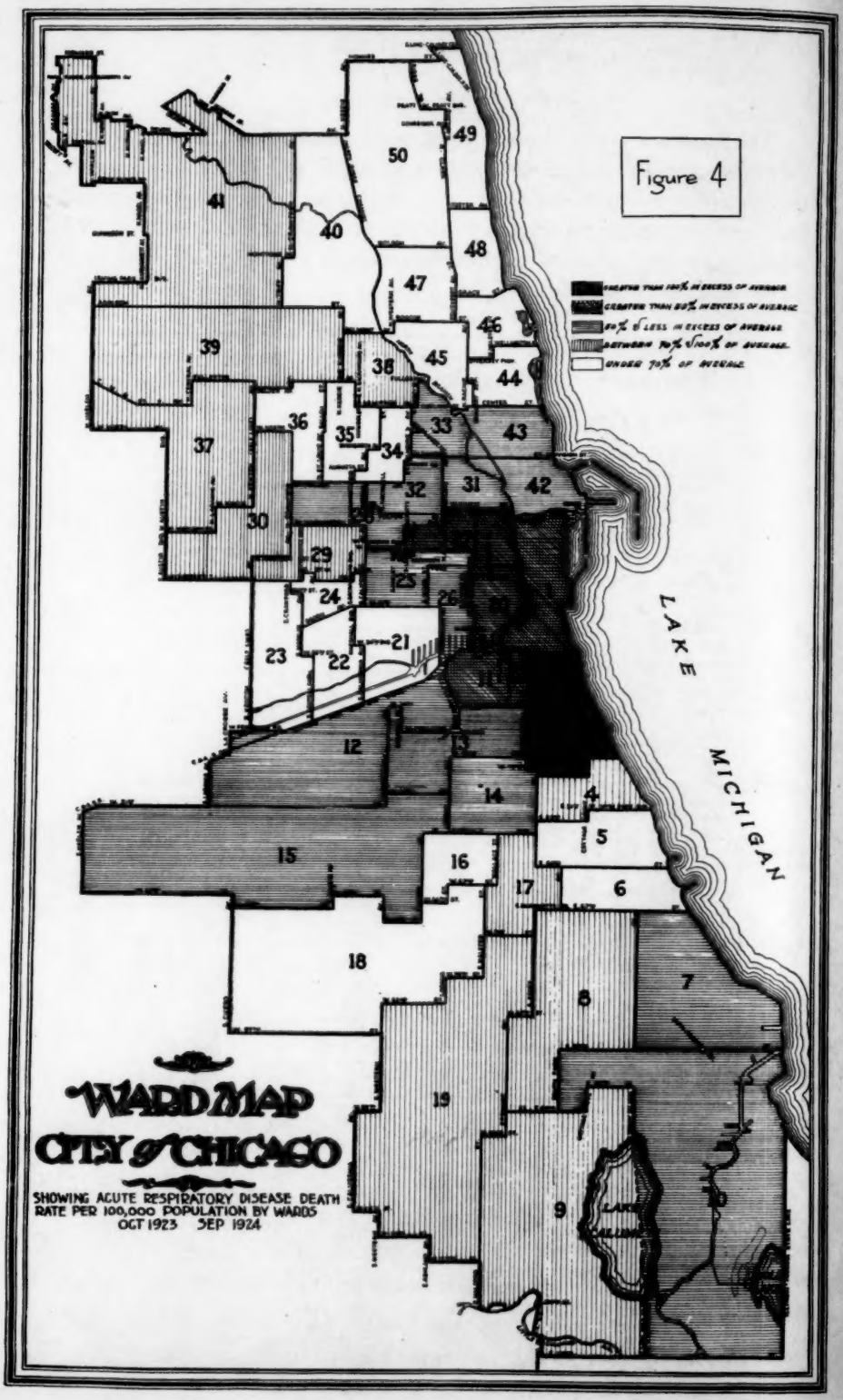
Figure 4
LAKE MICHIGAN
WARD MAP
CITY of CHICAGO
SHOWING ACUTE RESPIRATORY DISEASE DEATH RATE PER 100,000 POPULATION BY WARDS
OCT 1923 SEP 1924

1. Children suffering from acute coryza, sore throat or bronchitis should be excluded from attendance at kindergarten, and should be isolated in the home until recovered from such infection.

2. Vaccination against pneumonia as a protective measure is recommended in institutions for foundlings; in hospitals for babies under 2 years of age; in all patients with measles and whooping cough cared for in institutions and in all patients quarantined in the homes during the winter months; in patients with rickets, especially when affecting colored children.

TABLE 5.—*Anatomic Types Represented in Acute Respiratory Disease Deaths Children Under 5 Years of Age and All Ages October, 1923, to September, 1924*

	1923 Oct.-Dec.		1924 Jan.-March		1924 April-June		1924 July-Sept.		1923-1924 Oct.-Sept.	
	Under Five	All Ages	Under Five	All Ages	Under Five	All Ages	Under Five	All Ages	Under Five	All Ages
Lobar pneumonia	50	336	84	645	64	471	34	191	232	1,643
Bronchopneumonia, including capillary bronchitis	117	186	304	402	210	285	80	107	711	980
Acute bronchitis	40	47	61	62	43	54	22	26	166	189
Pneumonia, not defined, and influenza with pulmonary localization	10	37	20	62	11	47	3	7	44	153
Total	217	606	469	1,171	328	857	139	331	1,153	2,965

3. Diseased tonsils and nasal obstructions which interfere with free respiration should be removed.

4. In all cases of measles and whooping cough, the patients should be protected against persons who have acute coryza, coughs, sore throat or bronchitis.

5. Patients with measles and whooping cough complicated with pneumonia should be separated and isolated from patients not having such complications, and the room in which the patient is isolated should be maintained at a proper temperature, with the necessary humidity and ventilation.

RECURRENT RICKETS*

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It has long since been realized that rickets runs an irregular course, characterized by remissions and exacerbations. Physicians came to this conclusion as the result of direct clinical observation, which was confirmed more recently by a study of roentgenographic films; it is a point emphasized by Schmorl and other pathologists, as well as by those who investigated the mineral metabolism of this disorder. This striking irregularity in the progress of rickets is due to the fact that there are exceptionally many factors which tend to bring about fluctuations in its course; among this number may be mentioned starvation, exposure to a greater or less degree of sunlight, and variations in the diet. No doubt, there are still other factors which tend to alter the course of a disorder which at present appears so complex in its etiology. Although the frequent occurrence of relapses or remissions is well recognized, the incidence of recurrences is rarely mentioned. By recurrences, in contradistinction to relapses, we have in mind a clinical condition characterized by well defined and distinct attacks of rickets, separated by an interval free from all signs of active disorder. This complete intermission generally takes place during the summer months. The beading of the ribs subsides, the roentgenographic picture shows marked calcification of the epiphyses, the inorganic phosphorus and calcium content of the blood attain normal percentages, and the infant seems to have recovered completely and permanently. Some months later, generally in the course of the succeeding winter, the various signs and symptoms return, sometimes to a greater, although generally to a less degree.

The subject of recurrences incidentally involves the question of antirachitic treatment—what should be regarded as its proper duration and should it be discontinued after all clinical, chemical and roentgenographic signs have disappeared? It also raises the question of the action of the two specific remedies for rickets—cod liver oil and ultraviolet radiation—are these effective merely during the course of treatment and for a short period thereafter, or do they confer protection for many months? Another aspect concerns the age period which should be regarded as predisposing to rickets; is the current opinion correct which holds that susceptibility becomes greatly lessened after the first year or eighteen months of life?

On looking over the records of rickets of some years ago, of the period before cod liver oil was given as a routine procedure, I was much

* Received for publication, Nov. 11, 1925.

surprised to find how many instances of recurrences they contained. Incidentally it may be mentioned that this review has strengthened the conviction, expressed a number of years ago, that cod liver oil should be given as a routine prophylactic measure against rickets, in much the same way as orange juice or other antiscorbutic food is added to the dietary to prevent the development of latent or subacute scurvy. A total of thirty-one recurrences were noted, occurring during the first two years of life. It is difficult to estimate what percentage of cases this figure represents. In a clinical condition of this kind, a percentage figure tends to give a false impression, owing to the fact that there are so many contingent factors. For example, no infant may be considered as having escaped a recurrence of rickets unless he has been followed for a year or more—a period embracing at least two winters. Furthermore, all infants who receive cod liver oil, egg yolk, etc., during the first or second years of life must necessarily be excluded from the computation, as well as such as have failed to gain for one reason or another and have thereby temporarily acquired a partial immunity to rickets. When we reviewed our cases, bearing these factors in mind, it was surprising how frequently recurrences were encountered; in fact, few babies seemed to have escaped. It became evident that there is a great tendency for rickets to recur unless antirachitic treatment is given, and that the susceptibility to this disorder is almost as marked during the second as during the first year of life. This is not surprising when we consider that the second year is a period of exceptionally rapid growth, and that during this stage of life the infant is shielded from direct sunlight approximately to the same degree as during the first year.

It seems hardly necessary to cite all instances of recurrences, as, in general, they present similar outlines. I shall, therefore, confine this report to a summary of eight cases which serve to illustrate the salient features in this connection.

SUMMARY OF CASES

CASE 1.—F. W., in whom the first attack was definitely noted at 4½ months of age, in December. The beading and roentgenographic signs increased in spite of a diet of raw certified milk, and later the addition of 2 oz. of 20 per cent. cream for a period of three months. Absolute healing, as judged by the roentgenogram and by clinical signs, came about in May and June, and a recurrence took place in January of the next year when the baby was 17 months old. He was then a fine baby, weighing 22¼ pounds, having 8 teeth, walking independently and with good musculature. Again, the rachitic signs were evidenced by the roentgenographic picture and the clinical signs. Under appropriate ultraviolet therapy, complete cure was brought about.

CASE 2.—T. S., at 4 months of age, in December, showed unmistakable signs of rickets. The beading was exceptionally marked and the roentgenographic picture typical. Cod liver oil in the dosage of 1 teaspoonful three times a day was given throughout the winter and spring months; nevertheless, a recurrence came about. When the baby was 19 months of age (in March of the succeeding year) the beading recurred, the roentgenographic picture showed the character-

istics of rickets, and the inorganic blood phosphate was found to be 3.57 mg. per hundred cubic centimeters. This baby was getting dried milk from cows which had been out at pasture during the summer. All signs completely disappeared when the baby was exposed to the solar rays.

CASE 3.—I. C. was found to have signs of rickets on admission in May when 3 months old. It was the type characterized by a low percentage of calcium, 7.5 mg. per hundred cubic centimeters, and normal phosphorus, 4.18 mg. per hundred centimeters. The craniotabes was marked, the rosary and roentgenographic signs moderate. It may be added that two carpal centers were present at this time. All these signs of rickets rapidly disappeared when the baby was exposed to the sunlight, and by June the calcium had increased to 10.5 mg. and the phosphorus to 4.40 mg. per hundred cubic centimeters. Throughout the fall and succeeding winter the baby throve well on the routine formula of pasteurized milk. At 1 year the weight was 19 pounds. A recurrence was noted in April of the succeeding year when the baby was 14 months of age. The epiphyses were enlarged and the legs were moderately bowed. In this attack the phosphorus and not the calcium was diminished, the former being 3.4 mg. and the latter 11.2 mg. per hundred cubic centimeters. As soon as the diagnosis of rickets was established, the baby was treated with irradiations from the carbon arc lamp and all abnormal signs quickly disappeared.

CASE 4.—I. M. showed signs of rickets in May when at the age of 2 months. As in the previous instance, the calcium was low and the phosphorus normal, the former being 7.8 mg. and the latter 4.54 mg. per cubic hundred centimeters. There were the usual clinical and roentgenographic evidences of rickets. Carbon arc therapy was employed, the calcium rapidly returned to normal and other signs disappeared. Eleven months later, in April, when the baby was 13 months old, evidences of rickets again became manifest. As in the previous case, the type of rickets was found to be somewhat different in its recurrent form. Whereas in the first attack the calcium was low and the phosphorus normal, in the second attack the calcium was normal, 10.2 mg., and the phosphorus low, 3.8 mg. per hundred cubic centimeters. The recurrence likewise yielded rapidly to irradiation with ultraviolet light.

CASE 5.—W. L. was an exceptionally fine child. At 4 months of age, in the month of March, he showed signs of rickets, namely, beading of the ribs and characteristic roentgenographic changes. These abnormalities, however, disappeared. The baby throve well, and at 14 months weighed 25¼ pounds. During the course of the subsequent winter he developed rickets the second time. The beading recurred, the roentgenographic picture was characteristic and the inorganic phosphorus of the blood dropped to 3.47 mg. per hundred cubic centimeters, the calcium being normal. Referrence to this case has been made in another connection, attention being called to the fact that within a period of a few weeks the phosphorus rose to normal, 4 mg. per hundred cubic centimeters, whereas the calcium fell to 7.55 mg. per hundred cubic centimeters. The blood picture and clinical signs were all rendered normal by means of irradiations with the carbon arc lamp.

CASE 6.—B. G., when admitted to the institution in March, was only 2½ months of age, and showed definite evidences of rickets. There were beading of the ribs, roentgenographic signs and a diminished percentage of inorganic phosphorus (3.70 mg.). The mother showed a ++++ Wassermann reaction. All these signs disappeared with the advent of the sunshine in the month of May. A recurrence, however, became evident in November, with signs similar to those which attended the first attack. It may be added that the child had a large spleen at 3 months of age. The diet was a formula prepared from raw, certified milk. In view of the positive Wassermann test of the mother, the infant received bichlorid of mercury continuously from the age of 4 months. The recurrent attack of rickets likewise yielded to ultraviolet rays.

CASE 7.—A. R. was the youngest infant with rickets who has come to our attention. On admission in May, he was 3 weeks old. He showed evidences of

rickets, as judged by the roentgenographic picture (2 carpal centers were present), and marked craniotabes. As is usual in cases of rickets in May, the signs rapidly disappeared without any special treatment. In the month of November, when the baby was 6 months of age, the signs reappeared. The roentgenograms showed the characteristic lesions, as well as transverse lines, which are evidences of the healing process. The rosary was also definite. The general condition of the child was poor. He was treated with ultraviolet rays, and began to thrive with the subsidence of the rachitic signs.

CASE 8.—M. E. was admitted in February when 6 months of age, showing definite signs of rickets; the roentgenographic picture disclosed some transverse lines at the epiphyses. When 18 months of age, in February of the subsequent year, the child again showed rickets as judged by beading of the ribs, enlargement of the epiphyses and rachitic changes at the distal ends of the radius and of the ulna. These signs of rickets, like those of the first attack, disappeared as a result of ultraviolet irradiation. Much to our surprise, a routine examination during the following September, when the baby was 26 months of age, revealed a third attack of rickets, that is to say, a second recurrence. Again the evidence was definite both clinically and objectively, beading of the ribs and roentgenographic picture. Irradiation by means of the carbon arc lamp was instituted, and the third attack of rickets yielded as had the two others.

These cases illustrate various points in connection with recurrences of rickets. It would seem to be immaterial, from the standpoint of liability to a recurrence, whether the first attack had been cured by means of adequate doses of cod liver oil or by ultraviolet irradiation. For example, baby T. S. (Case 2) had received 3 teaspoonfuls of cod liver oil daily from the time he first developed rickets, at the age of 4 months, until he was 9 months of age. Nevertheless, rickets recurred late in the subsequent winter when he was 19 months old. In passing, attention may be called to Case 1 as demonstrating that the addition of cream to the diet is unable to prevent rickets; this baby, it will be noted, for a period of 3 months received 2 ounces of 20 per cent. cream daily, in addition to raw milk.

The temporary quality of ultraviolet therapy—its power to cure rickets but inability to prevent a subsequent recurrence—is well exemplified by the fourth case in the foregoing series. This baby also illustrates a phenomenon which has been noted in several instances, and which is difficult to explain—a first attack of rickets, characterized by a low percentage of calcium in the blood, and a second attack, occurring about a year later associated with a low percentage of inorganic phosphorus, the calcium content of the serum remaining normal. The same phenomenon of low calcium during one attack, and of a low phosphorus content of the blood in the recurrent attack, is brought out in the report of baby J. C. (Case 3). As is well known, this reversal in the type of rickets, viewed from a chemical standpoint, is frequently noted in the late spring when tetany supervenes on rickets. The inorganic phosphorus content of the blood or the plasma is low, when suddenly a shift takes place and it is found that the phosphorus has attained the normal percentage but that the calcium, heretofore normal in amount, has

become markedly diminished. This turn of events is illustrated in the recrudescence of Case 5.

The baby B. G. (Case 6) is included because the mother showed a positive Wassermann reaction, although, it may be added, the serum of the baby was negative in this respect. It is believed by some, especially by Marfan, that syphilis plays an important rôle in the etiology of rickets and, therefore, the recrudescence in this case may be attributable in part to this complication. It is difficult to appraise the rôle of syphilis in the etiology of rickets, although, in view of the widespread incidence of rickets, it seems evident that syphilis can play but a secondary part. From an observation of several cases, it has appeared to me that mercury tends to the development of rickets, and the recrudescence in this instance may have been associated etiologically with the giving of corrosive sublimate. The youngest case of rickets which we have seen is A. R. (Case 7), who showed roentgenographic signs of rickets at the age of 3 weeks, which signs became increasingly evident as time went on. This baby illustrates a point brought out by a study of the series, namely, that infants who develop rickets very early in life are particularly prone to develop recurrences within the first year. Of the five recurrences which took place during the first year of life, all were instances of early rickets. The last case of the series (Case 8) is significant in having developed rickets three times—in other words, having had two recurrences. The first attack was noted when the baby was 6 months of age, the second at 18 months, and the third at 26 months. The third recurrence was observed by chance in the course of a routine roentgenographic examination, and otherwise would have escaped attention, for the baby was thriving and appeared normal. This chance observation suggests that similar twofold recrudescences may occur more frequently than has been noted. As in this instance, they would be apt to take place during the third year of life.

A review of these cases brought out the surprising fact that of the total of thirty-one recurrences, twenty-five involved male infants and only six were in female infants. The paucity of cases precludes generalizing from these figures. Their divergence, however, is so great as to be striking, notwithstanding the fact that approximately two-thirds of the infants under observation were of the male sex. It is possible that the incidence of recurrences may, to some degree, serve as a delicate indicator of the comparative susceptibility of the sexes to rickets, and that males are somewhat more susceptible than females.

CONCLUSION

The broad conclusion to be drawn from these clinical observations is that recurrences of rickets are very frequent, especially during the

second year of life. Such being the case, it is clear that specific therapy —whether cod liver oil or ultraviolet irradiation—should be continued after all signs and symptoms of rickets have disappeared. Furthermore, cod liver oil should be given not only during the first, but also during the second winter. This is advisable particularly in regard to infants who have had rickets and who are, therefore, susceptible to a recurrence in the course of the subsequent winter.

THE VALUE OF NUTRITION CLASSES TO THE UNDERNOURISHED CHILD

A COMPARATIVE STUDY *

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In recent years, much stress has been placed on the importance of malnutrition on the health of the child. Physical defects, poor habits and improper home control have been assigned as causes of malnutrition. As a remedy, a so-called nutrition program has been outlined, which aims to correct these wrongs. The nutrition class has been introduced as one of these remedies.

In this study, malnutrition has been based on the height-weight relationship as compared with approved charts. Children with and without obvious physical defects were considered malnourished, provided they were more than 7 per cent under the normal as indicated by the table. It is conceded that malnutrition in its true meaning would include many children who measure up to the standard tables, but whose musculature shows every sign of poor nutrition, while so-called underweight children may have good musculature and be in excellent physical condition. With few exceptions, the scales determined in these children whether a child should be considered undernourished.

NUTRITION PROGRAM

Granting that malnutrition in children is an indication of physical inferiority and may predispose to infections, any program that aims to improve the nutrition of children is justifiable. Periodic weighing, physical examinations, correction of physical defects and health talks form the basis of all nutrition programs. The nutrition class, as conducted in Rochester, was introduced by Dr. W. R. P. Emerson of Boston, and the methods inaugurated by him were employed. From twenty to twenty-five children of about the same age who were 7 per cent, or more, underweight were organized into a class. Before they were admitted, permission was obtained from the parents in order to secure their interest and cooperation. This class met once a week, and was directed by a trained nutrition worker. Each child was given a complete physical examination by a competent physician. A weight chart for each member was kept, and advice was given as to diet, rest,

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* Study undertaken by the Department of Health Education of the public schools of Rochester.

fresh air and exercise. A parent was expected to attend the class as often as possible. These classes were conducted for different age groups in various schools in the city for a period of twenty weeks. Children who attained the desired goal in weight were spoken of as graduates. With such an organized nutrition class, definite results were anticipated. The complete physical examination given in the parents' presence would reveal remedial physical defects. When these were found, the child was referred either to the family physician or to the clinic. Many otherwise unrecognized defects might be found. The correction of physical defects, adjustment of the child's program, mainly out of school hours, increased or changed diet and stimulation by competition should offer the child the most favorable opportunity for gain in weight. Not only must the normal rate of gain be established, but the rate of gain must be accelerated in order to bring these so-called underweight children to normal. Experience with many children in the nutrition classes has shown that a large percentage of the children gain far in excess of the normal rate. In a study made on sixteen classes, with twenty children in each one, the average gain per child weekly was from 300 to 500 per cent of the normal gain. These apparently rapid and accelerated gains suggest that the nutrition class offers great hope for the undernourished child.

ULTIMATE RESULT OF GAIN

However, the query arises, what is the ultimate result of this accelerated gain? Do children hold the accumulated weight, and for how long? Do other children who are as much underweight, but who do not receive the same stimulation given in the nutrition class, make satisfactory gains ultimately? The real value of the nutrition class must be judged by answering these questions. In this study, an effort has been made to compare the immediate and late effects of the class on the nutrition of the child, with similar observations on a like group of malnourished children who did not receive the direct benefit of the class organization. Nutrition classes have been conducted in Rochester since 1921. As all children in the schools were weighed and measured twice a year, it was possible to secure an equal number of children for controls. Observations were made on groups taken at random so as to include children of different age groups and from the extremes of the social scale. Records were kept of the nutritional status of the child at the beginning of the nutrition class, at the closing of the class, at six and at twelve months, and in a smaller group at eighteen months after the termination of the class. Record was kept of the physical defects, corrected and uncorrected, and of the parents' cooperation. In all fairness, however, it must be stated that the control children, though not in the nutrition class, were in the same school. It was noted that the teach-

ings and the enthusiasm created in a nutrition class often permeated the entire school, so that the control children may have been definitely benefited by the class even though they were not enrolled.

FIRST STUDY

The first study was made on a group of 315 children who were in the nutrition class for a period of twenty weeks, and on an equal number of underweight children who were not in the nutrition class. During the class period, more than twice as many children gained as in the control group. Fifteen per cent of the class group graduated or reached the normal zone, while only 8 per cent of the control group did as well. In the class group, 69 per cent of the children improved, while only 28 per cent of the control group improved during the twenty weeks' period. The stimulation of the nutrition class definitely

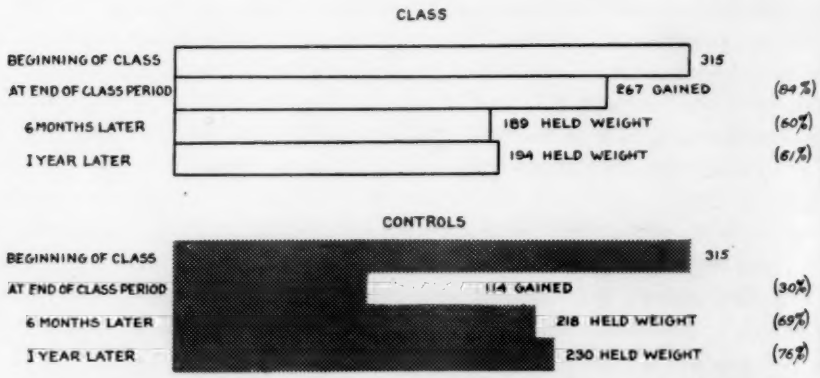

Chart 1.—The number of children in nutrition and control classes, who gained and held their weight for a year.

accelerated the gain during the class period, but, on weighing and measuring the children and the controls six months and one year later, the benefits of the class looked less favorable. At the end of six months, 189, or 60 per cent, of the children in the class group held the gain they had made, while in the control group, 218, or 69 per cent, of the 315 children held their gain, showing that more children in the control group gained during the six months period than in the class group. At the end of one year, 194, or 61 per cent, of the 315 class children held the gain made during the year, while 230, or 76 per cent, of the children in the control group held their gain made during the year. From this study it would seem that children stimulated by the class gained more rapidly than unstimulated children, but that the gains made by many of them are not held over a period of a year while the gains made by the control children are held. However, this study did not

reveal the percentage of gain in the groups considered, so another group of 317 class children and 317 control children were taken and the percentage of malnutrition in the two groups was ascertained over a period of one year.

The average percentage of malnutrition in the class group was 11 per cent, while that of the control group was 9 per cent. The class group at the end of the class period had reduced the malnutrition from 11 to 4.9 per cent, showing a reduction of 5.1 per cent. The control group had reduced the malnutrition over a similar period from 9 to 6.5 per cent, or a reduction of 2.5 per cent. At the end of six months the class group had lost 1.5 per cent of its gain with an average of 6.4 per cent malnutrition, while in the control group there was little loss, showing 6.8 per cent. At the end of a year the class group showed a slight gain, with a net gain of 4.8 per cent as compared to a net gain of 3.1 per cent in the control group. It is obvious in comparing these

TABLE 1.—*The Percentage of Malnutrition in the Class and Control Group Over Period of a Year*

Status	Class Group: 317 Children; Average Percentage Underweight, 11				Control Group: 317 Children; Average Percentage Underweight, 9			
	No. of Children	End of Class Period, per Cent	6 Mo. Later, per Cent	12 Mo. Later, per Cent	No. of Children	End of Class Period, per Cent	6 Mo. Later, per Cent	12 Mo. Later, per Cent
Graduates	38	0	6	5	28	0	2	2
Gained but did not graduate	274	7	8.5	8.3	89	6	7	6
Remained stationary	2	8	7	8.5	158	10	10	9
Lost	3	8.5	11	10.6	42	11	11	8
Average		4.9	6.5	6.2		6.5	6.8	5.9

two groups that the class gives an incentive to the child which yields a rapid gain in weight. Many more children make an initial gain than in the control group. It is true also that in subsequent months the class children suffer a greater loss of weight than those in the control group. This loss, however, is more than offset by the bigger initial gains and by the fact that children who might remain stationary or lose, do gain, though not rapidly enough to reach to the so-called normal zone.

SECOND STUDY

Another study was made on a group of 500 children who were in nutrition classes, and an equal number of control children. The group in the nutrition classes presented a poorer state of nutrition than the controls. There were sixty more children who were more than 15 per cent underweight in the class group. A survey of these children at the end of a year showed that children who were only slightly under normal did almost equally well in both groups. Among the children

who were 10 per cent underweight, there was a greater improvement at the end of a year in the class group, while in the children who were 15 per cent, or more, underweight there was a decided improvement in the class group over the controls. One must conclude from this series that the class made no great increase in the number of children attaining normal weight at the end of a year, but made a decided permanent improvement in children who were 10 per cent, and more, underweight. Compared with the controls these children showed considerable improvement. There can be little doubt that the class was of real benefit to them.

To answer the question of what happens to the so-called graduates of the nutrition class, a group of 161 graduates were followed for a year after the termination of the class. It was found that 105 were in

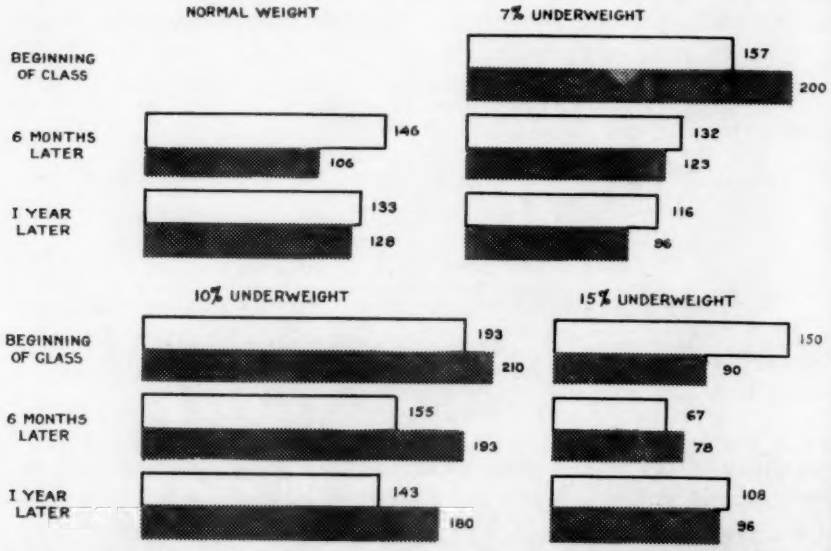

Chart 2.—The nutritional status of 500 children who had been in nutrition classes, and an equal number of control children at the beginning of the class, six months and one year later. The class is shown in white, and the controls in black.

the normal zone one year after graduation. In other words, 65 per cent of the children who reached the desired goal during the class period maintained this status at the end of a year. The other 35 per cent did not maintain the weight they acquired during the class period, but did not revert to their original condition. It is evident that the regulation of a child's habits may bring about a gain that is lasting, while a smaller percentage will gain under the stimulus of the class, but on returning to their accustomed activities will lose part of the accelerated gain.

What is the relationship between recognizable physical defects and the ability to gain weight? Much stress has been placed in nutrition class methods on the importance of correcting a child's physical defects to make them "free to gain" as Dr. Emerson terms it. In the 1,000 children studied who were entered in the nutrition classes, the six common physical defects found were: diseased tonsils and adenoids, defective eyesight, carious teeth, pulmonary defects (bronchitis and tuberculosis), cardiac deformities (mainly chronic endocarditis) and urinary disturbances (albuminuria and cystitis). Similiar physical defects were found in the group of control children. An attempt was made to correct as many of these defects as possible. The cooperation of the parents was earnestly sought, but it was not alway obtained. As a rule, children were kept in the nutrition class even if the apparent physical defect was not corrected. A survey of the children in whom

TABLE 2.—*Status of Graduates of Nutrition Classes at Beginning of Class and One Year After Graduation* *

	Normal	7% Under	10% Under	15% Under
At beginning of class	0	89 (55.5%)	64 (40%)	8 (4.5%)
One year after graduation	105 (65%)	22 (13%)	31 (19%)	3 (3%)

* One hundred and sixty-one graduates were followed.

TABLE 3.—*The Relation of Physical Defects to Ability to Gain Weight* *

Free to gain (free from obvious physical defects)	205	Average gain, 9.3 pounds Expected gain, 2.0 pounds
Not free to gain (obvious physical defects present)	117	Average gain, 9.5 pounds Expected gain, 1.9 pounds
Status at end of one year		Free to gain, 53% held weight Not free to gain, 54% held weight

* Three hundred and twenty-two graduates were followed.

the defects were corrected and left uncorrected was made. A group of 322 graduates of the nutrition classes was followed for a period of a year. An analysis of this group showed that the obvious physical defects were corrected in 205 children. These children were known as "free to gain." There were 117 children in the group who had obvious physical defects at the time of graduation. They were termed "not free to gain." The "free to gain" group had an average gain of 9.3 pounds during the class period, while the "not free to gain" had an average gain of 9.5 pounds. Out of the free to gain group 53 per cent held their weight at the end of a year, while 54 per cent of the "not free to gain" held their weight. This does in no way mitigate against the importance of correcting physical defects, because there were a number of striking instances in which a rapid and persistent gain followed the correction of a defect. It does mean, however, that some physical defects are in no way related to the state of nutrition.

PARENTS' COOPERATION

One of the most important factors stressed by Emerson in the nutrition class program is the cooperation of the parents in altering unfavorable conditions that may be a factor in retarding the child's normal growth. To assure a child sufficient rest, lessen or regulate outside activities and supervise the child's diet, are beyond the nutrition workers' control unless the parents cooperate. This necessary cooperation and interest is not easily obtained. Parents will frequently cooperate early in the class period and then their interest relaxes. To determine if good home cooperation was a factor in the class children, a group of 1,112 children were studied. It was found that, out of the 111 graduates, good home cooperation was obtained in 67 per cent, while in 958 children who gained but could not reach the normal zone good home cooperation was obtained in 44 per cent of the children. In the small groups of children who remained stationary or lost, good home cooperation was obtained in only 35 per cent. It cannot be denied that the parents' interest and help is an important factor in improving a child's nutrition, and failure to gain, as is anticipated, may be due to improper social conditions.

TABLE 4.—*The Relationship of Parents' Cooperation to Gain of Weight in 1,112 Nutrition Class Children*

	Number	Good Home Cooperation	Poor Home Cooperation
Graduates	111	75 or 67%	36 or 33%
Gained but did not graduate	958	423 or 44%	535 or 56%
Remained stationary	23	8 or 35%	15 or 65%
Lost weight	20	7 or 35%	13 or 65%

COMMENT

It is generally accepted that malnutrition in children, as determined by the height-weight relationship, is an undesirable condition. If this assertion is correct, efforts to improve the nutrition of a child are justifiable and desirable. The nutrition class has been introduced as a means of reaching this goal. The immediate results obtained in a class are most encouraging. The ultimate results are less encouraging, but are still better than in the groups in which no concentrated effort was made. The underlying cause of a child's poor nutrition is not always easily ascertained. The obvious thing may not be the cause. Based on an analysis of our material, remedial physical defects are a factor in only about 50 per cent of the children. The regulation of home conditions is an outstanding factor in promoting better nutrition. The greatest number of lasting gains were made in children in whom the importance of rest was stressed and heeded, longer sleeping hours and curtailed activities. The nutrition class was able to bring to the parents' attention the importance of this phase of the program. It is

in this field that the class exerted its greatest influence on the rest of the grade and school. No other method of combating this problem has brought it so forcibly home to the parents as when they attend a class, and study the charts of the class with the nutrition worker or physician. The possible causes for failure to gain are mentioned, and the interested and sympathetic parent may be aided in adjusting the home program. On the other hand, the problem of malnutrition is not solved by the establishment of nutrition classes. In spite of the help given many children who attended the classes, new recruits are found each year, some of whom were well nourished a year before. The benefits of the class nutrition program must be given to all school children, in order to encourage the well nourished child to remain so. This method is now being adopted in the schools. The principles of the nutrition class are applied to the entire school and one class is conducted in the school for the extreme and problem cases. Whether the results gained by this combined method will be any better cannot be ascertained for several years.

CONCLUSIONS

1. Nutrition classes, as introduced by Emerson, offer a way for children to receive instruction, which will cause an accelerated gain in about 80 per cent of the children enrolled.

2. Similiar gains in equally poorly nourished children not in nutrition classes were made by 35 per cent of the children.

3. Gain in weight made by children in nutrition classes was not held as well as gains made by children in the control group, not in classes, at the end of a year.

4. Big initial gains made by children in the nutrition class reduced malnutrition in the class group 4.8 per cent. The gain made by control groups reduced malnutrition 3.1 per cent at the end of a year.

5. Nutrition classes have greater permanent benefit to the children who are more than 10 per cent underweight than for those only slightly underweight.

6. Physical defects do not necessarily bear a relation to the state of nutrition. The term "free to gain" if related to physical defects is misleading.

7. The best results in the nutrition class can be obtained if the parents cooperate in regulating the child's habits.

8. Nutrition classes have had a beneficial effect on other members of the school, for the teachings of the class have been carried by the pupils to their families and friends.

9. Nutrition classes have been the means of correcting many physical defects in children, from which the child will benefit, even though the nutrition was not brought to normal.

10. Nutrition classes have introduced a concrete and effective method of teaching health habits that have a wholesome value on a child, irrespective of the nutrition.

11. Nutrition classes alone are not likely to eradicate malnutrition. They are an aid to its correction.

12. Nutrition classes deserve an important place in the nutrition program of schools. The ultimate result shows that 45 per cent of the gain acquired during the class period is lost. But the 55 per cent permanent improvement is about one-third better than that made by similiarly malnourished children who received only general health instruction, but who did not have the stimulation of the class.

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PROGRESS IN PEDIATRICS

ACIDIFIED MILKS

WITH SPECIAL CONSIDERATION OF THE INDICATIONS AND LIMITATIONS TO THEIR USE *

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The recent literature on acidified milk in infant feeding has been repeatedly [1] reviewed in this journal, and therefore need not be summarized again.

The modification of cow's milk by the addition of acid is based on the high content of buffer substances in cow's milk, the resistance of which must be broken down before gastric digestion can proceed normally. The buffering property of milk was recognized first by Leo [2] in 1888, and was soon thereafter studied by Escherich [3] (1889), by Heubner [4] (1891), and by Müller [5] (1892). Müller found that it was two to three times as great in cow's milk as in human milk These workers employed the method of titrating with hydrochloric acid, using congo red (p_H range from 3 to 5) as an indicator. It was not until 1914 that the buffer curve of milk was charted according to hydrogen ion concentration. This was done by Aron [6] for both human and cow's milk, and the striking difference between the two was clearly defined. In the same year, Clark [7] noted the high buffer concentration of cow's milk, and called attention to the absurdity of lime water additions, which still further increased the difficulties of gastric digestion.

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1. Moffett, R. D.: Review of the Literature for 1923 on Infant Feeding, Am. J. Dis. Child. **27**:618 (June) 1924. Holmes, J. B.: Recent Work in Anatomy, Physiology and Pathology of Infancy and Childhood, Am. J. Dis. Child. **29**: 650 (June) 1925. Moffett, R. D.: Review of the Literature on Infant Feeding for 1924, Am. J. Dis. Child. **30**:700 (Nov.) 1925.

2. Leo, H.: Ueber die Funktion des normalen and kranken Magens und die therapeutischen Erfolge der Magenspülung im Säuglingsalter, Klin. Wchnschr. **25**: 981, 1888.

3. Escherich, T.: Beitrag zur Pathogenese der bacteriellen Magen-und Darmkrankheiten. Verhandl. d. Gesellsch. f. Kinderh. zu Heidelberg **9**:109, 1889.

4. Heubner, O.: Ueber das Verhalten der Säuren während der Magenverdauung der Säuglinge, Jahrb. f. Kinderh. **27**:32, 1891.

5. Müller: Zur Kenntniss des Verhaltens von Milch und Casein zur Salzsäure, Jahrb. f. Kinderh. **34**:439, 1892.

6. Aron, H.: Das Salzsäurebindungsvermögen von Frauen-und Kuhmilch, Jahrb. f. Kinderh. **79**:288, 1914.

7. Clark, W. M.: The Reaction of Cow's Milk Modified for Infant Feeding, J. M. Res. **31**:431, 1914.

In spite of the early discovery of these facts, the logical inference, that acid might be directly added to cow's milk to lessen the digestive burden on the stomach, was not put into practice for nearly thirty years. This is the more surprising since buttermilk was introduced into medical practice by de Jager[8] in 1895, and was said by him to have been a popular practice in Friesland since 1770. The use of buttermilk for various digestive disturbances, especially diarrhea, became popular in Germany in the early years of the twentieth century, and has been in general use by pediatricians throughout the world up to the present time. A modification of this type of food, Finkelstein's protein milk, introduced in 1910, is still the best known and most widely used dietary means of treating severe diarrheas in infancy.

Klotz,[9] in 1909, was perhaps the first to administer to infants a milk to which acid as such had been added. In a series of experiments to determine the metabolic effects of lactic acid, he gave from 1.0 to 8.0 Gm. of lactic acid daily in skimmed milk (the exact amount of milk is not stated), and determined in a control experiment that the effects of buttermilk and of skimmed milk to which lactic acid had been added to about the same point of acidity were apparently identical. Klotz, however, in spite of the fact that some of the infants throve during the experiment, failed to suggest that acidified milk might be of practical value in infant feeding.

Marriott,[10] in 1922, called attention to the lessened gastric digestive capacity of sick infants, and advised the use of concentrated milk sufficiently acid to be readily attacked by the gastric ferments (bacterially soured milk).

Scheer,[11] in February, 1922, in the treatment of tetany, reported the use of a mixture of 740 cc. of raw cow's milk and 260 cc. of tenth normal hydrochloric acid. Eight infants between the ages of 6 and 13 months received this mixture, seven of them taking 1,000 cc. of this mixture daily, and another taking 800 cc. Apart from the beneficial effect on the tetany, it was noted that the infants took the mixture well and had good alkaline stools (p_H 7.46). The amount of acid was chosen because it brought the reaction approximately to that obtaining in the stomach at the height of digestion (p_H 4.58). No untoward symptoms were noted, and in a later paper, Scheer,

8. De Jager, L.: Karnemelk als voedsel voor kinderen beneden het jaar, Nederl. Tijdsch. v. Geneesk. **31**:679 (Oct.) 1895.

9. Klotz, M.: Milchsäure und Sauglingsstoffwechsel, Jahrb. f. Kinderh. **70**: 1, 1909.

10. Marriott, W. McK.; Davidson, L. T., and Harshman, L. P.: Studies on the Digestion in Infancy. I. Hydrogen Ion Concentration of the Gastric Contents, Tr. Am. Pediat. Soc. **34**:39, 1922.

11. Scheer, K.: Die Beeinflussbarkeit der Spasmophilie durch Salzsäuremilch, Jahrb. f. Kinderh. **97**:130 (Feb.) 1922.

Müller and Salomon [12] reported that, using still larger quantities of acid (400 cc. of tenth normal hydrochloric acid daily), no harm resulted even when, as in one case, it was given for three months. Scheer did not propose the use of acidified milk for other purposes than the treatment of tetany.

In June, 1923, Faber [13] read a paper on hydrochloric acid milk, in which he discussed the principles of debuffering cow's milk with acid additions, and their practical application in infant feeding, and reported a series of cases in which acidified milk had been fed with success. In the discussion of this paper, Marriott announced that he had been using lactic acid additions to cow's milk instead of a bacterially soured milk, and later, he and Davidson published a detailed report [14] of the method and its results.

Since then, Hess and Matzner [15] have proposed the use of citric acid (lemon juice), and Dunham [16] of acetic acid (vinegar) for souring milk. Both methods, as well as those of Faber and Marriott, appear to have given good clinical results. Marriott's method is the one at present most widely used.

RELATION OF ACID FEEDING TO ENZYME ACTION

The dependence of enzyme action on hydrogen ion concentration was established by Sorensen.[17] The optimal p_H for the various ferments was studied by him, and somewhat later by Davidsohn,[18] and more recently by Sherman and others.[19] The more important references will be found in previous papers.

The function of gastric acid is to produce a concentration of hydrogen ions in the ingested food, which will be optimal for the action of

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12. Scheer, K.; Müller, F., and Salomon, A.: Zur Pathogenese und Therapie der Tetanie. III. Experimentelle Untersuchungen über Salzsäuremilch, Jahrb. f. Kinderh. **106**:85, 1924.

13. Faber, H. K.: Hydrochloric Acid Milk in Infant Feeding. Am. J. Dis. Child. **26**:401 (Nov.) 1923; Tr. Am. Pediat. Soc. **35**:74, 1923.

14. Marriott, W. McK., and Davidson, L. T.: The Acidity of the Gastric Contents of Infants, Am. J. Dis. Child. **26**:542 (Dec.) 1923.

15. Hess, A. F., and Matzner, M. J.: The Value of Milk Acidified with Lemon Juice: Its Combination with Egg Yolk to Add the Antirachitic Factor, J. A. M. A. **82**:1604 (May 17) 1924.

16. Dunham, B. S.: Acidification of Milk with Vinegar (Acetic Acid) in Infant Feeding, Am. J. Dis. Child. **29**:200 (Feb.) 1925.

17. Sorensen, S. P. L.: Enzym-studien. II. Über die Messung und die Bedeutung der Wasserstoffionenkonzentration bei enzymatischen Prozessen. Biochem. Ztschr. **21**:131.

18. Davidsohn, H.: Die Pepsinverdauung im Säuglingsmagen unter Berücksichtigung der Acidität, Ztschr. f. Kinderh. **4**:208, 1912; Ueber die Abhängigkeit der Lipase von der Wasserstoffionenkonzentration, Biochem. Ztschr. **49**:249, 1913.

19. Sherman, H. C.; Thomas, A. W., and Baldwin, M. E.: Influence of Hydrogen Ion Concentration Upon Enzyme Activity of Three Typical Amylases, J. Am. Chem. Soc. **41**:231, 1919.

the gastric ferments. The acid itself may split cane sugar and perhaps to a slight extent protein. The three chief gastric enzymes are (*a*) rennet, (*b*) lipase and (*c*) pepsin. The ranges of optimal hydrogen ion concentration are different for the three. For rennet, the range is $p_H \pm 5.0$; for gastric lipase, p_H 4.0 to 5.0; for pepsin, p_H 2.0 to 2.8. Under normal conditions, the food is gradually brought from an alkaline or approximately neutral reaction for most foods, excepting some fruits, to a markedly acid reaction (p_H 3.0 to 4.0), thus passing through the optimal ranges for rennin and lipase, but not quite attaining that of pepsin. After passage into the small intestine, the chyme is gradually alkalinized by sodium carbonate of the pancreatic secretion, and by the absorption of carbon dioxid by the intestinal mucosa and passes through the optimal ranges, which are on the alkaline side, of the pancreatic and intestinal enzymes. A high buffer content in the food delays the acidification of the gastric contents, and requires a greatly increased secretion of hydrochloric acid. Whether the subtraction of excessive amounts of chlorine from the blood stream (to accomplish this excessive hydrochloric acid secretion in the stomach) may sometimes cause unfavorable temporary effects on the acid base equilibrium of the blood in the direction of alkalosis is uncertain. *A priori,* this might be expected to present some dangers in tetany, latent or manifest.

While different acids act alike in reducing buffer values and in increasing hydrogen ion concentration, there are specific differences in the enzyme activating properties. Thus, Hammarsten [20] states:

> The rapidity of the pepsin digestion depends on several circumstances. Thus, different acids are unequal in their action; hydrochloric acid shows in slight concentration, from 0.8 to 1.8 parts per million, a more powerful action than any other acid, whether inorganic or organic. In greater concentration other acids may have a powerful action; but no constant relationship has been found between the strength of various acids and their action in pepsin digestion, and the statements in regard to the action of different acids are somewhat contradictory.

CHOICE OF ACID

The four acids—hydrochloric, lactic, citric and acetic—chiefly used in milk acidification, will be considered separately.

Hydrochloric Acid.—Earlier studies, as well as that of Stehle and McCarty [21] on the effects of administration of mineral acids on metabolism, are not strictly comparable with hydrochloric acid milk feeding, since the acid was given alone and without the compensatory feeding of bases, such as occurs when milk is also given. It is, however, of interest

20. Hammarsten, O.: A Textbook of Physiological Chemistry, Tr. by J. A. Mandel, Ed. 5, New York, John Wiley & Sons, 1908, p. 358.

21. Stehle, R. L., and McCarty, A. C.: The Effect of Hydrochloric Acid Ingestion Upon the Composition of the Urine in Man, J. Biol. Chem. **47**:315, 1921.

to note that one of the earlier studies (Walter [22]) showed that in the dog it was difficult to give enough hydrochloric acid to produce toxic effects (apart from local irritation of the stomach) because of the great capacity of the organism to neutralize it with ammonia.

Scheer, in 1922 [11] and 1924 [12] and Gamble, Ross and Tisdall [23] and Gamble and Ross [24] in 1923, studied the effect of hydrochloric acid in milk on the mineral and acid base metabolism. Gamble and Ross administered the equivalent of 750 cc. of tenth normal hydrochloric acid in milk to each of two infants over short periods of time (three days), and found that there was produced (*a*) an increased urinary elimination of water, total acids and bases, especially sodium and potassium; (*b*) a moderate reduction in the bound carbon dioxide of the plasma; (*c*) a moderate reduction of the plasma p_H (Cullen's method,[25] one case only); (*d*) an unaltered concentration of fixed base in the blood. Essentially what happens is, first, the passage into plasma of chlorine, which is then neutralized and excreted by the kidneys, carrying with it plasma water and its normal content of bases.

Gamble's experiments extended over a brief period, and only shows the primary adjustment of the organism to the absorption of an unoxidized acid. For our purposes, it is more important to know what the adjustment may be to long continued administration of such substances, in particular hydrochloric acid given in milk (hydrochloric acid, unlike other mineral acids, has no specific toxic properties). Unfortunately, no direct experiments on this point are available and one is forced to consider the probabilities.

On the basis of Gamble's observations, one may consider three possible conditions resulting from the continuing administration of hydrochloric acid:

1. An exhaustion of available fixed bases from the plasma might lead to the withdrawal of these substances from the intercellular, and finally from the intracellular, fluids.

2. There might occur an increased absorption of fixed base from the food and the establishment of a new mineral equilibrium, in which

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22. Walter, F.: Untersuchungen über die Wirkung der Säuren auf den Thierschen Organismus, Arch. f. exper. Path. u. Pharmakol. **7**:148, 1877.

23. Gamble, J. L.; Ross, G. S., and Tisdall, F. F.: Studies of Tetany. I. The Effect of Calcium Chloride Ingestion on the Acid Base Metabolism of Infants, Am. J. Dis. Child. **25**:455 (June) 1923.

24. Gamble, J. L., and Ross, G. S.: Studies on Tetany. II. The Effect of Ingestion of Hydrochloric Acid Producing Substances on the Acid Base Metabolism of an Infant and the Probable Manner of Their Action in the Treatment of Tetany, Am. J. Dis. Child. **25**:470 (June) 1923.

25. Cullen's method has been found unsatisfactory, and the change in plasma p_H though probable should perhaps be regarded as not yet demonstrated. (Bennett, M. A.: Proc. Soc. Exper. Biol. & Med. **33**:115 [Nov.] 1925.)

fixed base would flow more freely from the intestine through the plasma into the urine in sufficient quantities to carry with it the amount of acid (chlorine) absorbed.

3. Restriction of fixed base output by increased ammonia formation.

The first condition might readily occur if the supply of base in the ingesta were inadequate, and would lead to profound disturbances incompatible with life. Clinical experience has shown that such results do not occur with the amounts of hydrochloric acid fed over long periods of time.[12] Faber has fed hydrochloric acid milk over periods of more than four months.

The second condition may be expected to occur if an adequate supply of fixed base is present in the food, to supply the body's own needs for retention and the increased need for neutralization of chlorine.

An average of seven measurements by Langstein and Meyer [26] shows that on cow's milk feeding normal infants retain approximately 33 per cent of ingested sodium and 22 per cent of ingested potassium. Cow's milk contains [27] 59.8 mg. of sodium and 152 mg. of potassium per hundred cubic centimeters. (These figures are from Holt and Howland.) Applying the figures for retention, there would be an excess over the body's actual needs of about 40 mg. of sodium and 118 mg. of potassium from each 100 cc. of milk ingested. Together, these amounts would be capable of combining with approximately 176 mg. of chlorine, or the amount contained in about 50 cc. of tenth normal hydrochloric acid. Magnesium and calcium would take care of a small additional amount.

It may, therefore, be concluded that the amounts of acid prescribed by Faber (25 cc. of tenth normal hydrochloric acid to each hundred cubic centimeters of milk) have an adequate margin of safety in respect to fixed base. However, Scheer used amounts much in excess of this and of the apparent limits of safety (67 cc. of tenth normal hydrochloric acid per hundred cubic centimeters of milk), and Gamble and Ross, 75 cc. without apparent ill effects. Here we may assume that the ammonia protective mechanism had been called on heavily. Another and perhaps more likely explanation may be found in the experiments of Gamble, Ross and Tisdall. When hydrochloric acid is added to milk, chlorine combines with base to form salts, largely calcium chloride. The acid effect of calcium chloride is equal to only about 40 per cent of the equivalence in terms of normality of calcium chloride to hydrochloric acid.

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26. Langstein, L., and Meyer, L. F.: Säuglingsernährung und Sauglingsstoffwechsel, Ed. 2, Wiesbaden, J. F. Bergmann, 1914, p. 28.

27. Holt, L. E., and Howland, J.: The Diseases of Infancy and Childhood, Ed. 8, New York, D. Appleton & Co., 1922, p. 153.

The alkaline reserve of fixed carbon dioxide in the plasma is affected by the administration of hydrochloric acid. Gamble's figures show an approximate reduction of 40 per cent when 750 cc. of tenth normal hydrochloric acid is given, while Scheer, Salomon and Müller's show about 25 per cent reduction with 400 cc. The amount of acid given by Scheer and his co-workers is about three times, and by Gamble and Ross about four times, the maximum prescribed by Faber which, without direct measurements, may be assumed on the basis of a direct ratio to reduce the reserve by about 10 per cent.

In considering the relative merits of hydrochloric acid and organic acids, their effects on the absorption and retention of calcium deserve consideration. Under ordinary conditions, calcium appears to be absorbed with some difficulty (Sherman and Hawley),[28] and in amounts (witness the low normal calcium urinary excretion) little in excess of the needs for retention. Relatively mild hygienic defects (insufficient ultraviolet rays,[29] deficiency of the antirachitic principle, etc.) prevent adequate absorption. While the exact mechanism of calcium absorption is as yet unknown, it appears probable from the experiments of Telfer [30] and others that it depends on the presence of readily soluble calcium salts, and occurs only in a limited section of the upper gastro-intestinal tract in which the reaction is acid. Telfer suggests that the gastric hydrochloric acid is an important factor, since calcium chloride is the most soluble of the calcium salts, and that as the chyme passes down the intestine, chlorine is rapidly absorbed and the calcium returns to its highly insoluble phosphate and fatty acid combinations. Mason,[31] Salvesen, Hastings and McIntosh,[32] and Jansen [33] have shown that oral administration of calcium chloride causes a significant rise in the blood calcium while calcium lactate causes no significant rise. The rise is more marked when a calcium deficiency is present. Klotz showed

28. Sherman, H. C., and Hawley, E.: Calcium and Phosphorus Metabolism in Childhood, J. Biol. Chem. **53**:375 (Aug.) 1922.

29. Orr, W. J.; Holt, L. E., Jr.; Wilkins, L., and Boone, F. H.: Calcium and Phosphorus Metabolism in Rickets, Am. J. Dis. Child. **26**:362 (Oct.) 1923.

30. Telfer, S. V.: Studies on Calcium and Phosphorus Metabolism. III. The Absorption of Calcium and Phosphorus and Their Fixation in the Skeleton, Quart. J. Med. **67**:245 (April) 1924.

31. Mason, E. H.: A Note on the Absorption of Calcium Salts in Man, J. Biol. Chem. **47**:3, 1921.

32. Salvesen, H. A.; Hastings, A. B., and McIntosh, J. F.: Effect of Administration of Calcium Salts on Inorganic Composition of Blood, J. Biol. Chem. **60**:327, 1924.

33. Jansen, W. H.: Kalkstoffwechsel, Blutkalkgehalt und Kalkwirkung. Zugleich ein Beitrag zur biologischen Wertigheit verschiedener Kalksalze, nach experimentellen Untersuchungen am Menschen, Klin. Wchnsch. **3**:715, 1924; Kalkstudien am Menchen. IV. Das Verhalten des Blutkalks nach peroralen, subkutanen und intravenösen Kalkextragaben, Deutsch. Arch. f. klin. Med. **145**: 209, 1925.

that when from 4.0 to 8.0 Gm. of lactic acid was fed, there was a negative calcium balance. The data on this subject are fairly unanimous in showing that calcium absorption is better from calcium chloride than from organic salts.

Organic Acids.—It is generally assumed that ingested organic acids are completely burned in the body to carbon dioxide and water, and therefore involve no strain on the acid base equilibrium; and that no specific toxic effects need be feared. The rule, however, applies strictly only to a few, of which acetic acid is the most important. Oxalic and benzoic acids, for instance, are burned only to a small extent if at all; tartaric acid is largely unabsorbed; the fatty acids have to undergo elaborate transformations, and are only burned rapidly and completely under optimal conditions of carbohydrate utilization. The exact site of combustion is not known. It probably occurs in all actively metabolizing body cells and perhaps most actively in the liver and muscles. It may occur to some extent in the intestinal mucosa.

Lactic Acid.—It has been generally assumed that lactic acid in particular is rapidly and completely oxidized in the tissues and excreted as carbon dioxide and water without producing acidic or other effects on metabolism. The experiments performed by Klotz in 1909 showed that under certain conditions lactic acid definitely affects metabolism. Thus, in two healthy infants fed from 1.0 to 1.5 Gm. of lactic acid daily, there was an improved retention of nitrogen and minerals (in one, the ammonia excretion was increased 6.8 per cent); in a third, recovering from a gastro-intestinal disturbance, the absorption and retention of all these, as well as of the fat, was markedly diminished and a negative balance of calcium and magnesium occurred. In the fourth infant, three experimental periods were observed. During the first, when 1.5 Gm. of lactic acid was given daily, absorption and retention of all elements were improved. During the second, when 4.0 Gm. was given daily,[34] there was a reduced retention of ash, affecting potassium, sodium, calcium and magnesium. During the third period, when 8.0 Gm. was given, there was a markedly reduced retention of nitrogen and ash, potassium, while calcium and phosphorus showed negative balances. Fat absorption was notably diminished. Klotz's conclusions may be quoted. He says:

> The experimental series, as a whole, shows that in the child with a healthy gastro-intestinal tract, small doses of lactic acid tend to influence metabolism favorably. With increasing doses this toxic effect gradually lessens and leads finally to pathologic conditions which first attack the fat and mineral metabolism. . . . In any case, the experiments teach that lactic acid is no indifferent material; that even by small doses profound modifications of metabolism are effected.

34. This is the amount prescribed by Marriott for each 500 cc. of milk.

More recently, Blatherwick and Long [35] studied the effect on two young adults of the ingestion of bacterially soured milk (content of lactic acid estimated at 2 per cent). They found an increased urinary output of phosphorus and ammonia, an increased urinary acidity and in one case a reduction in the plasma carbon dioxide (the same phenomena as occur after hydrochloric acid administration). In agreement with other observers, they failed to find an increase in the organic acids of the urine. From their experiments it would appear that lactic acid, before it is completely metabolized, produces certain definite effects on the acid base metabolism not dissimilar to those of hydrochloric acid. From Klotz's experiments, one may infer that unfavorable effects may occur when as much as 4.0 Gm. of lactic acid daily is given to infants, but that half of this amount, or less, may be given safely and indeed with benefit.

Citric Acid.—There appear to be no direct metabolic studies of the effects of this acid on infants. Blatherwick and Long [35] found in young adults that, when large quantities of orange juice were taken, as much as 6 per cent of the ingested citric acid appeared in the urine as citrates, but without effect on the acidity or ammonia since the amount of base in the juice was sufficient to balance the acid during metabolism. This would presumably not be true of lemon juice, in which the ratio of acid to base is much higher. It remains to be seen what are the effects on the metabolism of infants of the amount of citric acid in lemon juice, as recommended by Hess. The clinical results appear to be excellent.

Acetic Acid.—Here again we have no direct metabolic experiments as guides. It is generally assumed, and so stated in the pharmacologic texts, that acetic acid is rapidly and completely burned in the body. Its salts are highly soluble. Gamble and Ross administered calcium acetate to an infant with tetany, and found a moderate increase in the blood calcium, though not so great as with calcium chloride. Marriott [14] states that acetic acid and citric acids in milk tend to cause diarrhea.

A disadvantage of the use of acids in the "natural" state (as in lemon juice and vinegar) is the variability in strength, as shown in table 1.[36]

It is, therefore, rather difficult to be sure of the degree of debuffering obtained by adding them to milk. Here vinegar is somewhat better since, as Dunham [16] recommends, large quantities can be laid in stock, and tested. It is difficult to carry out such a procedure with lemons.

35. Blatherwick, N. R., and Long, M. L.: Studies of Urinary Acidity; Effects of Drinking Large Amounts of Orange Juice and Sour Milk, J. Biol. Chem. **53**:103 (July) 1922.

36. The titrations were made by Miss Fannie Hadden in the laboratory of the Division of Pediatrics, Stanford Medical School.

In general, there appears to be no good reason why chemically pure acids should not be used instead of those in the natural state. Vitamins can be supplied separately.

Pending further investigation, there appears to be fewer objections to acetic than to the other organic acids for infant feeding.

AMOUNT OF ACID TO BE USED

In his paper, Faber advocated the use of a partly debuffered milk with the p_H but little altered. Nevertheless, pediatricians generally have followed Marriott in using much larger quantities of acid, such as not only largely debuffer the milk but lower its p_H to a considerable degree of actual

TABLE 1.—*The Variability in Strength of Acids in the Natural State*

	Cc. Tenth Normal NaOH*	Variation from Average
Cider Vinegar		
Sample 1	10.79	+32%
2	6.27	−28%
3	8.67	+ 6%
4	6.32	−29%
5	7.17	−12%
Malt Vinegar		
Sample 1	8.15	=
2	9.04	+12%
3	8.60	+ 5%
Grape Vinegar		
Sample 1	9.92	+21%
Distilled Vinegar		
Sample 1	8.24	+ 1%
2	6.60	−19%
Average of all samples	8.16	
Lemons		
1 (large)	8.40 †	−16%
2 (large)	9.60	− 4%
3 (large)	9.31	− 7%
4 (small)	9.15	− 8%
5 (small)	10.23	+ 3%
6 (small)	10.26	+ 3%
7 (small)	12.08	+21%
8 (small)	9.13	− 8%
9 (small)	11.88	+19%
Average	9.97	

* Required to neutralize 1 cc. of vinegar.
† Required to neutralize 1 cc. of expressed juice.

acidity. I still believe strongly that, as a general rule, the partial debuffering is the more physiologic and practically preferable method. The reasons for this, though based mainly on theoretic grounds rather than on direct experimental observations (which likewise holds for complete debuffering), deserve consideration. First, the purpose of debuffering in most cases is to remove an artificial obstacle to digestion inherent in cow's milk, and thus to simulate the conditions of natural feeding, rather than to introduce a predigested food into the stomach. The ingestion of a food already at or nearly at the maximum normal p_H of the stomach removes the need of, and hence the stimulus to, the normal secretion of hydrochloric acid in the gastric mucosa. For

routine feeding in cases of mild digestive disorder, certainly the use of a milk containing approximately the amount of buffers in human milk and hence requiring the normal secretory effort—no more and no less—for which the human stomach is adapted, is obviously the physiologic method par excellence. In conditions of marked lowering of the stomach's secretory ability, such as has been demonstrated by Marriott and others in marasmus, complete debuffering is doubtless logical and practically useful. Even here, a gradual reduction of acid additions should be attempted as clinical improvement occurs, for the purpose of permitting the stomach to return to its normal activity.

Another advantage of partial debuffering has already been touched on—the fact that the normal gradual progression of hydrogen ion concentration in the stomach under natural conditions, from approximate neutrality to a considerable degree of acidity, permits all the gastric ferments to exert their maximum effect in normal order.

By most writers, attention has been wholly focused on pepsin as the only gastric enzyme of importance. Yet rennet cleaves the casein molecule, and gastric lipase under normal conditions probably splits as much as 20 per cent of the ingested fat before it leaves the stomach,[37] while even the maximum normal acidity of the infant stomach is less than is required for the maximum activity of pepsin.

The superiority of hydrochloric acid over organic acids as an activator of pepsin and as a solvent of calcium combinations and a promoter of calcium absorption, has already been pointed out. If hydrochloric acid is not used as the acid additive before ingestion, it becomes doubly important that the stomach itself be encouraged to secrete as much hydrochloric acid as possible.

Finally, the partially debuffered milk, because of its practically unaltered taste, is taken freely and without objection by infants as contrasted with the customary "hold out" of most infants for one to three days against the ingestion of highly acid, completely debuffered milk.

Practical experience has convinced me that, excepting in very marantic infants, partial debuffering gives satisfactory results.

EFFECT ON FAT ABSORPTION

Clinically, one of the most striking results of feeding milk which has been bacterially or artificially soured, is the change in the stools. In infants who previously had diarrhea, the stools frequently become firm, smooth and pasty. In many instances, sour milk causes the stools

37. Convincing proof has been furnished by Davidsohn (Biochem. Ztschr. **45**: 284, 1912) that gastric lipase is a separate entity from pancreatic lipase, acting at a quite different p_H range.

to become bulky, dry and constipated. These characteristic changes are due to an increase in soaps, particularly in calcium soaps, and suggest that the action of the acid must be intimately related to fat digestion. Faber has suggested that the most probable explanation is an increase in soluble calcium compounds in the stomach, both as the result of the added acid, resulting in an increased combination of fatty acids and calcium to form insoluble and presumably indigestible soaps. Whether or not this is the true explanation, the increased output of calcium soaps in the stools must affect the percentage utilization of fat unfavorably in the normal child, though not necessarily so in the infant with diarrhea, since as Holt [38] has shown there is already poor absorption and greatly increased fecal loss of fats when diarrhea is present. Fat absorption under acid milk feeding has been little studied by direct experiment. The data in table 2 throw some light on the process.

TABLE 2.—*Data Collected from Klotz's Study*

Experiment	Fat Absorption, per Cent	Soap, per Cent in Stools	Calcium Retention
2. (a) Preliminary period	19.6	50.8	6.9
(b) + 1.5 Gm. lactic acid daily	39.5	23.5	6.4
3. (a) Preliminary period	94.6	9.1	32.2
(b) + 1.5 Gm. lactic acid daily	73.6	61.8	Neg. balance
4. (a) Preliminary period	67.9	45.4	Neg. balance
(b) + 1.5 Gm. lactic acid	86.1	22.9	19.7
(c) + 4.0 Gm. lactic acid	84.9	34.3	12.4
(d) + 8.0 Gm. lactic acid	73.7	50.6	Neg. balance

In general, the data show an inverse relationship between fat absorption and the percentage of soaps in the stools and also calcium retention. Lactic acid in small amounts improved the fat absorption in experiments 2 and 4, but in both instances this was abnormally low during the preliminary period and was not raised to the normal figure (from 90 to 98 per cent) during the period of acid feeding. In experiment 3, when fat absorption was normal during the preliminary period, lactic acid reduced it by over 20 per cent.

It seems fair to conclude that acid administration reduces fat absorption in normal infants, improves it when it has been previously low but does not restore it to normal figures. The inference may be tentatively made that acid feeding is not indicated for the routine feeding of healthy infants, but should be considered chiefly as a therapeutic method for use over a limited period until the disorder has been corrected.

38. Holt, L. E.; Courtney, A. M., and Fales, H. L.: The Chemical Composition of Diarrheal as Compared with Normal Stools in Infants, Am. J. Dis. Child. **9**:213 (March) 1915.

INDICATIONS FOR USE

Diarrhea.—Finkelstein's original ascription of a large group of diarrheas to sugar intolerance and fermentation as the primary causative factor, is now recognized as erroneous. While fermentation of carbohydrates frequently occurs, of course, it is in most cases secondary to imperfect enzymatic action or to increased peristalsis, which in turn is secondary to a systemic disorder (general infection). The essential factor is the admittance of undigested carbohydrate into the lower reaches of the bowel, in which heavy bacterial contamination is present. Another group of cases of diarrhea may be due, as Marriott thinks, to capillary damage in the bowel from circulating streptococcal toxins, causing an efflux of water, serum and sometimes blood; if this is the case, no regulation of diet will exert any direct beneficial effects on the disease. In the first group, however, the facilitation of gastric and duodenal digestion should have a direct beneficial effect. While Finkelstein's theory may be faulty, clinical experience has abundantly demonstrated that his albumin milk is a highly effective therapeutic agent. This milk has a relatively high acidity and low buffer action, and in all probability these properties have much more to do with its effects than have its relatively low content of sugar and soluble salts. More recent experience with acidified milks has shown somewhat similar effects, whether hydrochloric, lactic, citric or acetic acid has been used. Our own experience has convinced us that a partly debuffered milk has, except in the most severe cases, as good an effect as the wholly debuffered.

Celiac Disease.—In this disease (chronic intestinal indigestion), the high protein diet in general use, consisting as it does largely of casein, has a very high buffer value, and gives a specific indication for the use of acid. Protein milk is therefore a logical food and forms a part of most celiac diets. If the amount of sugar remaining in skimmed milk can be tolerated, artificial souring may be employed. During convalescence, acid may also facilitate the reintroduction of fat into the diet.

Marasmus.—Marriott and others have shown that here the secretory capacity of the stomach for hydrochloric acid is much diminished and that acidified milk improves digestion and promotes gain in weight. Here a fully debuffered milk is indicated at first and partly debuffered milk during convalescence.

Routine Feeding.—For routine feeding of healthy infants, we neither practice nor advocate the use of debuffered milk. It should be remembered that the adaptive powers of the average healthy infant are such that he can easily meet the extra demands on gastric secretion made by the ingestion of cow's milk. With a short preliminary period of gradual habituation, whole undiluted cow's milk can sometimes be taken by them

at surprisingly early ages. For most infants who are given clean milk cleanly handled, simple dilution with additions of carbohydrate gives such uniformly good results that the further complication of formula preparation is both unnecessary and annoying to mothers and to nurses. In my opinion, therefore, acidified milk should be used only for infants with digestive disorders or conditions predisposing to them; and for those with tetany and perhaps rickets.

For young and premature infants, acidified milk may at times be useful. In an earlier paper, I objected to the use of acidified milk in very early infancy, largely on theoretic grounds that gastric digestion was negligible at that age. Recently, Griswold and Shohl [39] found that there is an active secretion of hydrochloric acid in the new-born, but came to the same conclusion as I did, namely, that alkaline food was preferable at early ages. While our observation that colostrum, the normal food of the new-born, is fairly alkaline is undisputed, we nevertheless have found, in agreement with Marriott and others, that even highly acidified milk is apparently well borne by very young infants and may be used—preferably only for brief periods—when a high caloric food of small volume is desirable.

Tetany.—Scheer's use of hydrochloric acid in milk in treatment of tetany is well known. Scheer now uses 400 cc. of tenth normal hydrochloric acid to 600 cc. of whole milk. Freudenberg and György [40] consider that tetany is due to a low ionization of calcium [41] in the blood, while Gamble and his associates find that the effectiveness of chlorine in the treatment of tetany is probably due to an increased ionization of the blood calcium.

The chief and a quite important advantage of hydrochloric acid milk over the calcium and ammonium chlorides is its greater palatability and lack of unpleasant by-effects.

Rickets.—In 1922, Zucker and his co-workers [42] found that an excess of acid ions prevented rickets in rats when added to a rickets producing diet. Jones [43] found that a diet with a basic ash (such as that of cow's milk) predisposed puppies to rickets, while an acid ash did not have this effect. On the other hand, Boget and Kirkpatrick [44]

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39. Griswold, C., and Shohl, A. T.: Gastric Digestion in New-Born Infants, Am. J. Dis. Child. **30**:541 (Oct.) 1925.

40. Freudenberg, E., and György, P.: Tetanie und Alkalosis, Klin. Wchnschr. **2**:1539, 1923.

41. Zahn, in 1922, was able to demonstrate this directly in one of his patients by perfusion experiments (Monatschr. f. Kinderh. **24**:45, 1922).

42. Zucker, T. F.; Johnson, W. C., and Barnett, M.: The Acid Base Ratio of the Diet in Rickets Production, Proc. Soc. Exp. Biol. & Med. **20**:20, 1922.

43. Jones, M. R.: Hydrochloric Acid Therapy in Rickets, J. A. M. A. **82**:439 (Feb. 9) 1924.

44. Boget, L. J., and Kirkpatrick, E. E.: Studies in Inorganic Metabolism. II. Effects of Acid Forming and Base Forming Diets on Calcium Metabolism, J. Biol. Chem. **54**:375, 1922.

found that calcium is retained better on a basic than on balanced or acid forming diets; György [45] thinks there is a tendency to acidosis in rickets, and Burgess and Osman actually demonstrated a lowering of the plasma bicarbonate. The probably superior absorption of calcium on hydrochloric acid rather than organic acid administration, has already been discussed. It is possible, however, that this may be overbalanced by an increased excretion.

Acidification of the urine in pyelitis is necessary when hexamethylenamine is given. This acidification is usually accomplished with an acid such as benzoic or acid forming salt, such as calcium chloride or acid sodium phosphate. Hydrochloric acid in milk gives the same effect in a more palatable and less disturbing form. One gram of calcium chloride corresponds with 180 cc. of tenth normal hydrochloric acid in chlorine content, and to about 72 cc. of tenth normal hydrochloric acid in its acidifying effect on the urine (Gamble).

In achlorhydria, particularly in pernicious anemia, hydrochloric acid milk has been found useful.[46]

CONCLUSION

On the basis of the available studies, acidified milk may be considered to be a useful therapeutic agent for certain specific disorders. As such, it should be given only when there are specific indications, and for periods of time limited by the regression of symptoms. Organic as well as inorganic acids deflect metabolism from the normal to a recognizable, though not as yet fully determined extent. For this reason, the routine use of sour milk in the feeding of normal infants is not to be encouraged. For them, modification of cow's milk by dilution and carbohydrate addition remains the method of choice.

45. György, P.: Ueber Rachitis und Tetanie, Jahrb. f. Kinderh. **102**:145, 1923.

46. Personal communication from the medical service of Lane Hospital, San Francisco.

News and Comment

PROF. CESARE CATTANEO HONORED

This journal is in receipt of a volume announcing the twenty-fifth anniversary of the granting of professorship to Prof. Cesare Cattaneo, the eminent Italian pediatrician. This volume contains a short sketch of Professor Cattaneo's life, together with two addresses which he has delivered on pediatric subjects; the first in 1900 at the University of Parma on the "Character and Importance of Pediatrics"; the second, his inaugural address at the University of Milan in November, 1925. The volume also contains a complete bibliography of Professor Cattaneo's publications and those of his students.

Abstracts from Current Literature

Anatomy and Physiology

THE SUGAR CONTENT OF THE BLOOD. BEN K. HARNED, J. Biol. Chem. **65**:555 (Oct.) 1925.

The Folin-Wu method of determining blood sugar is believed by Benedict to give results about 25 per cent too high, due to the presence of reducing substances in the blood other than glucose. The author, precipitating the proteins of the blood with mercuric nitrate and freeing the blood of all nitrogen other than nitrate, obtained results similar to those obtained previously by Benedict. The author does not recommend his method as a routine procedure for blood sugar determination, as it is quite laborious and exacting.

HIGGINS, Cincinnati.

Pathology, Bacteriology and Biochemistry

CAUSE OF NITRITOID CRISIS FOLLOWING INTRAVENOUS INJECTION OF ARSENICALS. ERNEST FRIEDRICH MÜLLER, Arch. Dermat. & Syph. **12**:349 (Sept.) 1925.

Previous publications by the author and co-workers have shown that all persons react to arsphenamine injections by a transient lowering of the number of leukocytes in the peripheral blood. In those patients who developed a nitritoid crisis as the result of arsphenamine injection, the leukopenia was marked. In patients not developing a nitritoid crisis, leukopenia could be prevented by epinephrin injection. The nitritoid crisis was attributed to an abnormal reaction of the involuntary nervous system. Further, it was observed that silver arsphenamine injection was not followed by a nitritoid reaction, though it was followed by a leukopenia in those in whom a nitritoid reaction developed after arsphenamine injection.

Widal's hemoclastic crisis consists of the development of a transient leukopenia following the ingestion of milk on an empty stomach. It was believed by Widal to occur as a result of liver disease. The author found that the ingestion of milk on an empty stomach gave results entirely similar to those occurring after the intravenous injection of silver arsphenamine. The "crisis" occurred in patients in whom there was no suspicion of liver disease, but who had reacted to arsphenamine injection with a nitritoid crisis. "This confirms former conclusions that the unusual reaction in the blood following injections of silver arsphenamine into patients, who also show symptoms of a nitritoid crisis after administration of arsphenamine, is not due to the drug, but rather to a pathologic reactivity of the involuntary nervous system. This abnormal reactivity, latent in the body itself, is due to a disturbance of the involuntary nervous system."

SODIUM CHLORID IN THE TREATMENT OF BROMISM. JAMES STEVENSON, Arch. Dermat. & Syph. **12**:525 (Oct.) 1925.

Wile's previous observation that sodium chloride administered intravenously hastens the excretion of bromide is confirmed. In an experiment on himself,

the author shows that sodium chloride is equally effective when taken by mouth, and that the increased excretion of bromide is not due to diuresis.

JEANS, Iowa City.

ON THE DISTRIBUTION OF INJECTED SULPHATES IN TISSUES. W. DENIS and STELLA LECHE, J. Biol. Chem. **65**:565 (Oct.) 1925.

Hypertonic solutions of sodium sulphate were injected intravenously into dogs; the sulphate was almost wholly excreted in the urine, essentially none being absorbed by the various organs of the body.

A FURTHER INVESTIGATION OF THE CHEMICAL PROPERTIES OF INSULIN. D. A. SCOTT, J. Biol. Chem. **65**:601 (Oct.) 1925.

The author prepared pure insulin, which was a snow-white powder and contained 25,000 units per gram. This product was analyzed and found to contain 50.40 per cent carbon, 6.62 per cent hydrogen, 14 per cent nitrogen, 4 per cent ash. Insulin seems to be a protein in that it is destroyed (1) by trypsin, and (2) by specific reagents as formaldehyde, nitrous acid, benzol chloride and carbon disulphide, and because the nitrogen content is similar to that of a true protein. Insulin contains little tryptophane, little cystine, considerable tyrosine, a high amide content and low humin nitrogen.

THE INFLUENCE OF ORALLY ADMINISTERED CALCIUM SALTS ON THE SERUM CALCIUM OF NORMAL AND THYREOPARATHYROPRIVIC DOGS. AXEL M. HJORT, J. Biol. Chem. **65**:783 (Oct.) 1925.

The author fed solutions of calcium to dogs, lactate, calcium chloride and calcium glycerophosphate and found an increase of the calcium of the blood serum. The dose of calcium lactate used was 225 grains for a dog weighing 10 Kg. Smaller doses were without effect. The author prefers calcium lactate to calcium chloride, as the latter in equivalent doses caused vomiting.

(The large doses of calcium lactate necessary to raise the calcium of the blood explains its inefficiency in treating tetany in infants as compared to calcium chloride. Abstractor.)

HIGGINS, Cincinnati.

THE INFLUENCE OF HIGH PROTEIN DIET ON THE KIDNEYS. A. JAMES MILLER, J. Exper. Med. **42**:897, 1925.

Six groups of young, adult, albino rats were fed on diets containing fat, carbohydrate, protein, salt and accessory food substances with the proportion of the ingredients varied so that the protein content for group 1 was 1.36 per cent; group 2, 9.56 per cent; group 3, 20.17 per cent; group 4, 29.89 per cent; group 5, 28.76 per cent; and for group 6, 40.13 per cent.

The left kidney was removed from one rat in each group except group 1, thus doubling the work of the remaining kidney. The food was given ad libitum. After 6 months blood urea nitrogen determinations were made, all remaining animals were killed and examined. Group 3 served as a control.

A seventh group of sixteen pied rats was fed cooked lean beef and whole milk, three additional ones on stock room diet served as controls. Blood uric acid was determined at the beginning and end of the nine weeks feeding period. The animals were then killed and examined.

Results.—The blood uric acid and blood urea nitrogen determinations and microscopic examination revealed no evidence of kidney damage. There was

evidence of kidney hypertrophy consisting of increased weight of the kidney, larger diameter of the capillary tufts, convoluted tubules and kidneys in the rats on high protein diets.

The nephrectomized rats on high protein diets had no kidney changes except hypertrophy.

McClure, Evanston, Ill.

Isolation of Bacteriophage Free from Bacterial Proteins. Lloyd Arnold and Emil Weiss, J. Infect. Dis. **37**:411 (Nov.) 1925.

The authors found that it was not possible to absorb completely the dissolved antigenic bacterial proteins from bacteriophage with the homologous bacterial antiserum. A method is outlined by which a filtrate free from antigenic bacterial proteins but containing a strong lytic substance was prepared from a bacteriophage.

The Reaction of Lung Tissue to Tuberculous Infection in Vitro. F. J. Lang, J. Infect. Dis. **37**:432 (Nov.) 1925.

In cultures of lung tissue inoculated with tubercle bacilli, both tissue cells and bacilli can be kept alive for a long time in a state of peculiar symbiosis (twenty-one days). Similar to the phenomena observed in human phthisis, the tissue shows, in response to the infection with tubercle bacilli, either a productive or an exudative reaction. This reaction is connected exclusively with cellular elements of the interstitial connective tissue of the parenchyma of the lung. This tissue contains (the hematogenous cells of the circulating blood being ruled out in cultures) two cell types; (1) the endothelium of the capillaries, and (2) the elements which the author describes as "septal cells," which are identical with the "granular" or "vacuolated" nucleated cells of the authors and are usually supposed to belong to the "respiratory epithelium." The endothelium of the capillaries, contrary to Foot, who believed the epithelioid cells of the lung tubercle and the large exudate cells of the exudative phthisis originated from the capillary endothelium, does not play any rôle. The epithelium is of no importance either, as the alveolar wall, according to previous investigations of the author, is not provided with any special "respiratory" epithelial layer, except the non-nucleated plates.

The septal cells are the real active elements. Together with the cells which were activated previously (dust cells on alveolar phagocytes) and correspond to the mobilized histiocytes in other parts of the body, for instance, in the omentum, they are mobilized and furnish the new free phagocytic and ameboid cells, engulfing the bacilli and transforming themselves into large epithelioid cells.

The epithelioid cells either accumulate in the alveoli in the form of large exudate cells or they become arranged in clusters like tubercle, in some cases a peculiar diffuse mesenchyme-like transformation of the interstitial tissue takes place. The two latter phenomena may be looked on as the expression of a productive reaction.

The typical giant cells seen by Maximow in cultures of lymphoid tissue with tubercle bacilli could not be found in cultures of lung tissue. Nevertheless, it is certain that in tuberculosis of the lungs the same elements must play the leading rôle as in tuberculosis of the lung in vitro. In the organism the hematogenous cells take a part in the process. It is known that they emigrate in all inflammatory processes and become transformed into polyblasts, and, in tubercle formation, furnish a part of the epithelioid cells.

The bronchial epithelium in many cases covers a part or a whole of the free surface of the explant; despite the proximity of large masses of tubercle bacilli and of widespread caseation of the underlying tissue, it may remain alive for a long time, and its cilia were seen beating in the latest stages observed. In the interior of the explant it forms cysts or solid islands, embedded in mesenchyme-like tissue or in necrotic masses.

The tubercle bacilli in the tissue cultures were found to influence the elements of the explanted tissue through their soluble products of metabolism. This influence may manifest itself locally as well as diffusely; to this action may be attributed the extensive mesenchyme-like tissue formation, especially in later stages, in which the toxins must be present everywhere in the culture in a uniform concentration.

In the cultures of lymphoid tissue with tubercle bacilli, the fibroblasts and the endothelium of the blood vessels assume an embryonic character. In the cultures of the lung the same is true for the septal cells of the interstitial connective tissue. They must be endowed with the unspent embryonic potencies and represent cells of a primitive, undifferentiated nature. They might be compared with the syncytial cellular reticulum of the lymphoid tissue or with the reticulo-endothelial, histiocytic elements of the organism in general. Under the influence of the stimulus originating in the tubercle bacilli, the septal cells which have not been used in the formation of wandering phagocytic elements (histiocytes, epithelioid cells) become transformed into a peculiar tissue, resembling embryonic mesenchyme. Under the conditions prevailing in vitro, they usually do not give rise to fibroblasts. In the organism, however, they might play a decisive rôle in the healing of the tuberculous lesions, in the substitution of the histiocytic reaction by the fibroblastic reaction, as a source of the fibroblasts forming the scar tissue.

KENNEDY, Rochester, Minn.

SEPARATION OF A SOLUBLE SPECIFIC SUBSTANCE FROM HEMOLYTIC STREPTOCOCCI. EDWIN F. HIRSCH, J. Infect. Dis. **37**:523 (Dec.) 1925.

A method is described for the extraction of a soluble specific substance from hemolytic streptococci. The chemical reactions of this substance resemble those of similar substances prepared from many bacteria by other investigators. Solutions of this substance give precipitin reactions in high dilution with antistreptococcus serums, and with the serum of rabbits injected with the substance.

OBSERVATION ON CASTELLANI'S FERMENTATION PHENOMENON. JUAN MANUEL FIALLOS, J. Trop. Med. **28**:426 (Dec. 1) 1925.

The writer cites some experiments of his own confirming Castellani's phenomenon. When certain organisms, which produce neither acid nor gas on carbohydrate mediums, are added to other organisms which produce acid but not gas, and the combination inoculated to carbohydrate mediums, both acid and gas are formed. For example, the *B. typhosus* on maltose produces acid, but no gas; the *B. morgani* produces on maltose neither acid nor gas; a combination of these organisms on maltose produces both acid and gas. No explanation is made for the phenomenon.

SCOTT, Philadelphia.

CELLULAR REACTION AND PHAGOCYTOSIS IN THE NORMAL AND IMMUNIZED GUINEA-PIG. S. METALNIKOV and K. TOUMANOFF, Ann. de l'Inst. Pasteur **39**:909 (Nov.) 1925.

Through a study of the cellular reaction of an animal to the injection of foreign substances, these authors maintain that several conclusions are justified as to the mechanism of immunity. In the nonimmunized animal, invasion is followed by the mobilization of white cells at the site of inoculation; the polymorphonuclear cells are the first to appear, followed in the course of hours by increasing numbers of large mononuclear and lymphocyte cells, unless the infection results in death within the first few hours. The polymorphonuclear cells continue to increase in number, and phagocytosis is quite marked until the invasion is checked or death supervenes. In the case of immunized animals, there is a similar preliminary increase of polymorphonuclear cells, but this and the phagocytic activity are checked sooner than in the normal animal.

The cellular formula differs rather characteristically with the type of invading organism. It also is modified by immunization. There is evidence that the cells themselves develop specific immunity, since washed white cells from immune animals show properties of resistance against the organism in question either in vitro or when injected into a nonimmunized host. The epiploic appendages and omentum also develop powers of specific immunity. Correlating the facts at hand with analogous biologic concepts, the authors conclude that immunity is a property developed by each tissue of the body, depends on alterations produced within the cell in response to the initial invasion, and that with successive invasions, all cells of the body are mobilized to combat the invading organism.

BOYD, Iowa City.

PITUITARY EXTRACT CAUSING HYPERGLYCEMIA IN INFANTS. W. STERN, Med. Klin. **21**:1011, 1925.

Injection of pituitary extract in infants produces a hyperglycemia after about an hour. In three hours the blood sugar returns to the initial level in older healthy infants. In the first three months of life of many infants, the blood sugar values are higher after this time.

In rachitic and athreptic infants, there is an apparent hyperglycemia present, due to the stronger and longer lasting hydremia. The experiments seem to support the theory of an extrarenal action of pituitary extract.

THE INFLUENCE OF CALCIUM AND POTASSIUM IONS ON THE ACTION OF INSULIN. ESKIL KYLIN, Med. Klin. **21**:1262, 1925.

The blood sugar curve was followed in a number of cases after the injection of insulin, and on two different days the same experiment was repeated after a previous injection of potassium chloride and calcium chloride, respectively.

The conclusions of the author are, that calcium ion, epinephrin, and sympathetic nervous system on one side, and potassium ion, insulin and vagus nerve on the other side, take the position of antagonists. The three different parts of these vegetative systems, that is, the electrolytes, hormones and the autonomous nervous system, combine their effects mutually. This means that in the same system they reinforce their action, while from system to system they reduce or neutralize it.

ZENTAY, St. Louis.

Nutrition

STUDIES IN CARBOHYDRATE METABOLISM. II. INVESTIGATIONS INTO THE MUTAROTATION OF β-GLUCOSE UNDER VARIOUS CONDITIONS. III. INVESTIGATIONS INTO THE NATURE OF THE GLUCOSE IN THE BLOOD OF NORMAL INDIVIDUALS. IV. INVESTIGATIONS INTO THE NATURE OF THE GLUCOSE IN THE BLOOD OF PATIENTS WITH DIABETES MELLITUS AND OF PATIENTS WITH BENIGN GLYCOSURIA. V. INVESTIGATIONS INTO THE FORM OF GLUCOSE IN DIFFERENT BODY FLUIDS. CHRISTEN LUNDSGAARD and SVEND AAGE HOLBØLL, J. Biol. Chem. **65**:305, 323, 343 and 363 (Sept.) 1925.

Glucose ordinarily consists of a mixture of two sugars, which are called alpha-glucose and beta-glucose. Alpha-glucose has a specific rotary power to light of + 10 degrees, while beta-glucose has a specific rotary power of + 19 degrees. When glucose is dissolved in water, the specific rotary power at first is high, due to a predominance of alpha-glucose, but after the solution has stood for several hours, there is some change in the sugar molecules so that the specific rotary power becomes + 52.5 degrees, and remains at this figure; the solution then contains 36 per cent alpha-glucose and 64 per cent beta-glucose. The authors experimented with beta-glucose and found that solutions of this sugar increased in specific rotary power to + 52.5 degrees, during the course of three hours, indicating the formation of some alpha-glucose.

A mixture of muscle tissue, insulin and glucose solution (+ 52.5 degrees) caused the specific rotary power of the sugar to diminish to approximately + 47.25 degrees. The authors believed that the lowering of the rotary power was not due to a change of some alpha-glucose to beta-glucose, because a solution of beta-glucose, insulin and muscle tissue yielded a sugar solution of higher specific rotary power than the original solution. The sugar probably contained gamma-glucose, or as the authors called it "new-glucose."

The authors developed a technic for obtaining the specific rotary power of blood sugar. Determinations of the specific rotary power of the sugar of the blood of (1) normal persons, fasting, (2) normal persons up to one hour after ingesting 100 Gm. glucose, (3) patients with diabetes mellitus with glycosuria, (4) patients with diabetes mellitus under treatment, (5) patients with diabetes mellitus after administration of insulin and (6) patients with benign glycosuria are given in the following table.

1. + 26.6, + 27.6, + 40.8 degrees. Average + 31.7 degrees.
2. + 37.9, + 33.2, + 31.0, + 26.3, 34.8, + 25.6, + 16.7, + 29.0, + 32.8, + 28.8, + 31.3 degrees. Average + 29.8 degrees.
3. + 50.4, + 52.0, + 50.8, + 51.2, + 50.8, + 51.5, + 50.9, + 50.9, + 51.5 degrees. Average + 51.1 degrees.
4. + 44.7, + 33.7 degrees. Average + 39.2 degrees.
5. + 34.4, + 38.4, + 41.4, + 26.9, + 43.0 degrees. Average + 36.8 degrees.
6. + 29.3, + 33.7 degrees. Average + 31.5 degrees.

The specific rotary power of the sugar of spinal fluid, edema fluid and pleural fluid was determined and is given in the following table.

Spinal fluid: + 14.1, + 14.8, + 23.6, + 22.4, + 18.1, + 13.2 degrees. Average + 17.7 degrees.
Edema fluid: + 10.4 degrees.
Pleural fluid: + 32.6 degrees.

Diabetic blood shows essentially the same mixture of alpha-glucose and beta-glucose, as found in a solution of glucose in water while nondiabetic blood

and body fluids show the presence of gamma-glucose or new-glucose, as found to less extent in the mixture of glucose, muscle tissue and insulin in vitro. It would thus appear that the formation of gamma-glucose or new-glucose, with a specific rotary power apparently less than that of beta-glucose, is an essential and probably the first link in normal carbohydrate metabolism, and that insulin is a necessary factor in its production.

Is the Antirachitic Factor of Cod Liver Oil, When Mixed with Ground Grains, Destroyed Through Storage? E. B. Hart, H. Steenbock and S. Lepkovsky, J. Biol. Chem. **65**:561 (Oct.) 1925.

Cod liver oil was mixed with ground grains and kept in the dark at room temperature for six months. The grain without the cod liver oil was fed to chickens and produced rickets, while chickens which received the grain with the oil did not develop rickets. Vitamin D of cod liver oil is quite resistant in contradistinction to vitamin A, which is easily destroyed by heat, light or oxidation.

The Nutritional Requirement of the Chicken. V. The Influence of Ultraviolet Light on the Production, Hatchability, and Fertility of the Egg. E. B. Hart, H. Steenbock, S. Lepkovsky, S. W. F. Kletzien, J. G. Halpin and O. N. Johnson, J. Biol. Chem. **65**:579 (Oct.) 1925.

Hens require either an antirachitic factor in the diet, or exposure to ultraviolet light (sunlight or irradiation) for satisfactory production of eggs. There is more lime in the shell of the eggs, if the hens are irradiated or receive cod liver oil; this not only increases the marketability of the egg, but affords more calcium for the growing embryo; the embryos of eggs of irradiated hens contain about twice as much lime when hatched as do the embryos from eggs of non-irradiated hens. The yolks of the eggs from irradiated hens contain ten times as much antirachitic property as the yolks of eggs of nonirradiated hens. Although irradiation of the hen does not increase the fertility of her eggs, yet the hatchability of the egg is greatly increased.

Higgins, Cincinnati.

Tissue Changes Following Deprivation of Fat-Soluble A Vitamin. S. Burt Wolbach and Percy R. Howe, J. Exper. Med. **42**:753, 1925.

Albino rats kept on a diet deficient in fat-soluble A vitamin developed specific tissue changes, consisting of substitution of stratified keratinizing epithelium for the normal epithelium in various parts of the respiratory tract, alimentary tract, eyes, para-ocular glands, and genito-urinary tract.

In general, the changes appeared first in the respiratory mucosa in the nares, trachea and bronchi, then in the salivary glands, eye and genito-urinary tract, then in para-ocular glands and pancreas. Exceptions to this order occurred. There were no changes in the epithelium of the liver, stomach, intestines and kidney.

The replacement of epithelium is shown by study of morphologic sequences to result from focal proliferation of cells arising from the original epithelium and not by differentiation or change of preexisting cells.

There is evidence that the growth activity of the epithelium is greatly augmented. In a few animals the behavior of the replacing epithelium in respect to numbers of mitotic figures and response on the part of connective tissue and blood vessels suggested the acquisition of neoplastic properties.

Other important effects of the fat-soluble A deficiency were atrophy of glandular organs, emaciation, localized edema of testes, submaxillary gland and connective tissue structures of the lungs, and focal myocardial lesions.

Histologic changes occurred more promptly and more extensively in immature than in full grown rats.

Control rats on the same diet, but with butter fat in place of lard, grew normally and were maintained in normal healthy condition for a year.

STUDIES ON EXPERIMENTAL RICKETS. I. THE OCCURRENCE OF RICKETS IN YOUNG RABBITS BORN OF MOTHERS INFECTED WITH SCHISTOSOMUM JAPONICUM. R. KAWAMURA and Y. KASAMA, J. Exper. Med. **42**:793, 1925.

Female rabbits were experimentally infected with *Schistosomum japonicum*. Some survived and became pregnant. The experimental and normal control animals were fed the same diet, and to all appearances both groups ate equally well and no evidence of a deficiency was noted.

Young rabbits born of the normal mothers grew at a normal rate, whereas 67.7 per cent of those born of infected mothers showed retarded growth, and the development of signs of rickets between twenty-five and thirty-five days after birth. The rickets was evidenced by enlarged and thickened wrists, ankles, knees, and costochondral junctions with fracture of ribs sometimes, and in some cases kyphoscoliotic disturbance of the vertebrae. Microscopic examination showed proliferation of the cartilage zone, thickening of unossified metaphyses, fibromatosis, and hyperemia of bone marrow in the epiphyses. The calcium of the bones was greatly reduced. The rickets reached its maximum in fifty to sixty days, and in ninety to one hundred days it had either declined or disappeared.

Two groups of affected young, aged 54 days, were selected, and to one group cod liver oil was administered daily. At the end of twenty-seven days the animals were killed and the left hind paws were examined. No evidence of rickets was found in the young getting cod liver oil, while the controls were still markedly rachitic.

When young healthy rabbits were infected with the parasite, slight signs of rachitic changes were noticeable within thirteen days and reached their maximum within thirty to sixty days.

MCCLURE, Evanston, Ill.

THE EFFECT OF SUNLIGHT ON GROWTH AND DEVELOPMENT. W. T. BOVIE, M. J. & Rec. **121**:65, 1925.

The author took 250 chickens and divided them into six lots. All received the same food and other treatment and all were housed in a greenhouse. Groups C and D received in addition green food and group F cod liver oil. Groups D and A ran out of doors in the day. Lots B and C were exposed to the light of a mercury vapor arc in quartz for twenty minutes daily. At the end of two months, A, B and C were well and sturdy and twice as tall as the other lots. Roentgenograms showed the legs were long, straight and well calcified. D and E were short and weak. The chickens in lot F were short but well calcified. A very narrow band of sunlight in the ultraviolet region of the spectrum does not pass through glass, but does pass through the quartz walls of the mercury vapor arc lamp. Hence A, B and C received the same rays of sunlight but by different means. Therefore the ultraviolet energy of sunlight is necessary for normal growth and development, and this part of

sunlight is also a protection against disease and even after disease has been contracted quickly, and permanently checks its progress.

A Review of an Important Problem in the Study of the Growth and Development of Children. Joseph H. Hidden, M. J. & Rec. **121**:743 (June 17) 1925.

It is now an established fact that iodine is an essential ingredient in our food for the maintenance of health, and that iodine poverty is not only felt by the general system but is the dominant factor in the causation of simple goiter. Boards of health are trying to devise means of administering it to the public. Placing a small percentage of iodine in our table salt seems to be the most popular measure proposed. Practicing physicians should be on the lookout for symptoms of iodine poverty in their patients, and should administer the drug before goiter develops or before myxedema or cretinism become evident. The symptoms in patients that suggest the need of iodine therapy are: (1) enlarged cervical glands; (2) inactivity, sleepiness, dulness; (3) weakness, obstinate constipation, distended abdomen; (4) coarse dry skin, scant or absent eyebrows, hair that has lost luster; (5) fingers that lack normal taper, teeth that are notched or show parallel ridges; (6) enlargement of thyroid.

Williamson, New Orleans.

Management of Summer Diarrhea. P. D. McCornack, Northwest Med. **24**:556 (Nov.) 1925.

McCornack says the morbidity and mortality of summer diarrhea in his state (Washington) is greater in September and October than in July and August, possibly because of the greater daily temperature variation. The usual type of diarrhea has a gradual onset and is easily controlled by proper dietary measures. This is frequently not done, because mothers fear a loss of weight and will not restrict the diet, with the result that an aggravated condition appears. Educational measures are necessary to prevent the feeding to infants of improper articles of diet, and feeding of spoiled and contaminated food. McCornack's dietary armamentarium is the usual one, consisting of boiled skim milk or protein milk, aided by the use of bismuth and paregoric.

Scott, Philadelphia.

Variations in the Blood and Urine Diastase Contents in Relation to Meals. J. Cohen, Brit. J. Exper. Path. **6**:173, 1925.

The diastase content of the blood is slight and quite constant, but the output in the urine is subject to great fluctuations. The ingestion of a meal usually causes an immediate increase in the diastase content of the urine, to be followed in some cases by a fall and in others by a continued high level. The author believes that the examination of isolated urine specimens for diastase concentration leads to very unreliable clinical information.

Hoag, New York.

Ultraviolet Light and the Antiscorbutic Vitamin. Philip Eggleton and Leslie J. Harris, Brit. M. J. **2**:998, 1925.

By experiments it was found that the antiscorbutic vitamin can be synthesized in complete darkness, and in their observations these investigators were unable to connect it in any particular whatever with ultraviolet light; in

contrast to this, the fat-soluble vitamins, on the other hand, have been shown to be affected by ultraviolet light in their synthesis and activation as well as in the prevention and cure of avitaminoses.

The practical significance of these results is to emphasize the importance of the provision of the C factor in dietaries. While it is possible to replace the fat soluble factors to some extent by light rays (either in the food or in the animal), the prevention of scurvy must rest with the supplying of the C factor in the food. It is of interest to note that of the numerous proprietary foods sold as substitutes for maternal feeding the authors were aware of only one that supplied the C factor.

BROWN, Toronto.

BASAL METABOLIC DETERMINATIONS IN TWO HUNDRED AND FIFTY WINNIPEG SCHOOL CHILDREN. A. T. CAMERON, Canad. M. A. J. **15**:1022 (Oct.) 1925.

Two hundred and fifty cases were examined in this series. Of these, eighty-six were normal and the remainder slight, moderate or marked goitrous cases. The Sanborn Handy apparatus was used throughout the tests. The definite technic is given in the article. The results showed the following predicted values in normal children:

Weight, Pounds	Oxygen Consumption per Minute	
	Boys	Girls
30	128	117
40	141	130
50	155	143
60	169	156
70	182	169
80	196	182
90	210	195
100	223	208
110	237	221

These values are higher than Benedict and Talbot's figures, the authors believing that the difference is due to the additional discomfort of the apparatus used by them and also to the higher metabolic rate induced by the greater amount of sunshine in Winnipeg.

Using these figures as a standard, they found that only 2.5 per cent. of the 163 goitrous children examined by them were definitely above maximum normal limits.

MOORE, Omaha.

A CONTRIBUTION TO THE PHYSIOLOGY OF WATER METABOLISM IN OBESE CHILDREN. RICHARD FRIESE and J. M. JAHR, Jahrb. f. Kinderh. **110**:205 (Oct.) 1925.

The conflicting ideas concerning the necessity of restricted fluid intake in the dietary management of the obese, is due to the paucity of our knowledge of the rôle of water metabolism in the production of increase or of decrease in weight. The relationship between the water and salt metabolism in normal and in obese children was determined and compared. The etiology of the obesity was not taken into account, but kidney function tests were made to avoid error. When water was given in large quantities, the fat children showed no greater tendency to retain fluids than did normal children. When Ringer's solution was given instead of plain water, the obese children showed a more protracted excretion than did the normal children; that is, the obese child appeared to retain a weak salt solution for a short time.

The twenty-four hour intake and output differed little in the two types of children. When water intake was considerably restricted, the normal children

showed a much smaller water output than did fat children. Also when diuretics were given, the fat child reacted much more fully than did the normal child. In other words, the water in the tissues of the fat child is much more labile than in the tissues of the normal child.

The author concludes that in the treatment of obesity little heed need be given to the water intake; the calories should be reduced to the minimum requirements, especially restricting the fats and carbohydrates and keeping the protein relatively high, giving rather large quantities of vegetables to give bulk without greatly increasing calories. A series of ten tables is appended, summing up the details of the various experiments.

PARMELEE, Chicago.

CLINICAL OBSERVATIONS WITH THICK CEREALS AS COMPLEMENTARY FEEDING OF INFANTS. P. GERSTL, Med. Klin. **21**:924, 1925.

Thick cereals are a good form of therapeutic feeding and very practical in mixed feeding.

This form of mixed feeding is indicated in habitual vomiting of infants, in case of unsatisfactory gaining in weight due to qualitative or quantitative deficiency of the mother's milk, also in exudative diathesis and in inanition dyspepsia.

The average gain in weight of infants fed by this method is better than of those fed by different methods. Infections do not occur more often in infants fed by this method, and the infections are not severer than in other infants. The beginning of mixed feeding of other kind was somewhat postponed and the period of nursing was lengthened by the method.

ZENTAY, St. Louis.

Prenatal Conditions

CONGENITAL CLEFT LIP. THOMAS F. MULLEN, M. J. & Rec. **122**:402 (Oct. 7) 1925.

Surgeons interested in reparation and corrective surgery seek to attain perfection from the anatomic and physiologic as well as from the cosmetic point of view. In the correction of congenital cleft lip, one has to close an unsightly gap in such a manner as to restore the function of the parts, and the closure must be planned to minimize visible scars, to give flexibility, fullness and length to the lip, and to restore symmetry of the nostrils. The best indication of time for operation is a consistent gain in weight, a good state of nutrition and absence of local infection. Correction of the alveolar deformity must precede every other operation. The cooperation of a pediatrician is vital to complete success. The patient should become accustomed to the nurse who is to take charge of him before operation. It is also important that the patient becomes accustomed to the method of feeding which will be used after the operation. Sucking should not be allowed for some time before or after the operation. The author then gives in detail the operation for this condition. After the operation the child should be kept quiet by any means. The mother should stay in the hospital with the infant and the breast milk pumped and fed with a sterile spoon or dropper at regular intervals. Examination is avoided as much as possible for the first few days and the lip and mouth syringed daily with sterile water.

WILLIAMSON, New Orleans.

CONGENITAL CARDIAC ANOMALIES. REPORT OF A CASE. B. G. MELLE and B. MELLE, South African M. J. **20**:315, 1925.

A male infant, who weighed 9½ pounds at birth, died during the second day of life with increasing cyanosis which began soon after birth. There was a harsh rasping sound in addition to the normal sounds lasting through most of systole and diastole. The child also had a complete cleft palate and lip and the feet were in eqinovarus position.

Necropsy showed the heart lying almost horizontal in the thorax, almost square shaped, the right side dilated and somewhat hypertrophied. The ductus arteriosus was widely patent and the left pulmonary artery seemed to arise from it; the lumen of the ductus was equal to the lumina of the two pulmonary arteries.

The great vessels seemed to be normal in position, but the isthmus of the aorta, that is, the part between the left subclavian artery and the ductus, was markedly stenosed and showed a peculiar twisting of the vessel wall, thus decreasing the lumen still further. The interauricular septum showed a marked defect.

EHRMANN, Chicago.

Diseases of the New-Born

INTRACRANIAL INJURIES IN THE NEW-BORN. C. H. RICHARDSON, JR., J. M. A. Georgia **14**:484, 1925.

The author thoroughly discusses the etiology, diagnosis, prevention, and treatment of intracranial injuries in the new-born. Early lumbar puncture as a diagnostic and therapeutic measure is recommended.

MASHBURN, Atlanta.

Acute Infections

FURTHER OBSERVATIONS ON THE USE OF THE ROENTGEN RAY IN PERTUSSIS. RALPH D. LEONARD, Am. J. Roentgenol. **13**:420 (May) 1925.

The results coincide with the results reported last year. Radiation produces a diminution in the number and severity of the paroxysms in over 75 per cent of cases, and usually controls the vomiting spells. Apparently greater effect is obtained in the young patients and by increased dosage. The results seem to be due to the effect on the bronchial glands.

STULIK, Chicago.

EFFECTS OF DIPHTHERIA TOXIN ON THE MYOCARDIUM OF GUINEA-PIGS. CARL W. APFELBACH, J. Infect. Dis. **37**:443 (Nov.) 1925.

The changes in the myocardium of guinea-pigs after injection of diphtheria toxin subcutaneously resemble the changes described in the myocardium in diphtheria in human beings, but they are usually not as extensive.

By direct injection of the myocardium, extensive degenerative and inflammatory changes can be produced in the guinea-pig equal in intensity to those found in human diphtheria. The outstanding changes are retrogressive (cloudy swelling, fatty change and necrosis). Infiltration of leukocytes with degenerative changes occur, but in the myocardium of guinea-pigs, degeneration, proliferation and exudation were not commonly observed together.

The degenerative changes in the skeletal muscles, liver and kidneys, as represented by the amount of fat that can be stained with sudan 3, are less than those in the myocardium.

KENNEDY, Rochester, Minn.

STUDIES OF YELLOW FEVER IN VERA CRUZ IN 1920-1921. THOMAS J. LEBLANC, J. Trop. Med. **28**:169 (May 1) 1925.

Seven cases of yellow fever were studied during the epidemic in Vera Cruz in the fall of 1920. Transmission of the disease to guinea-pigs was accomplished in one of the seven cases, and from the animals of the third generation a strain of *L. icteroides* was isolated in pure culture.

The strain induced in guinea-pigs produced all the typical symptoms of experimental yellow fever in this animal, namely, fever, intense jaundice and nephritis, hemorrhages into the gastro-intestinal tract, and degeneration and necrosis of liver and kidney.

Of seven patients with yellow fever treated with the anti-icteroides serum, all recovered except one, in whom treatment was delayed until the latter part of the third day of illness; that is, the mortality among treated cases was 14 per cent as against 43 per cent among untreated cases. The favorable effect of the treatment was evident within a few hours by the fall in temperature and pulse rate, and by the improved subjective condition of the patient.

Among 748 nonimmune persons vaccinated with killed cultures of *L. icteroides*, two cases suspicious of mild yellow fever occurred after the lapse of one month, while among unvaccinated nonimmune subjects 199 cases of yellow fever occurred. While the number of those nonimmune present in Vera Cruz is not accurately known, it could not have been large, because of the small foreign population of Vera Cruz and the comparatively recent occurrence of epidemic yellow fever, hence it is believed that the vaccination considerably reduced the incidence of the disease.

YELLOW FEVER RESEARCH, 1918-1924: A SUMMARY. HIDEYO NOGUCHI, J. Trop. Med. **28**:185 (May 15) 1925.

The properties of *Leptospira icteroides* are the same as those already demonstrated for the virus of yellow fever: it passes through bacterial filters; it is killed by a temperature of 50 C. maintained for five minutes; it is transmissible from man to animal and from animal to animal by means of infected female *Aedes aegypti* mosquitoes. *L. icteroides* is invisible under the ordinary microscope but visible by dark field illumination.

L. icteroides induces a symptom complex and pathologic changes in suitable experimental animals (young guinea-pigs, puppies and certain monkeys) which are identical with those of yellow fever.

Yellow fever and infectious jaundice are distinct, independent infections. They are quite similar in character.

L. icteroides is distinct, both morphologically and serologically from *L. icterohemorrhagia* of infectious jaundice and *L. hebdomadis* of seven day fever.

The prophylactic value of the vaccine prepared with killed cultures of *L. icteroides* and the efficacy of the anti-icteroides immune serum prepared in horses were demonstrated in animal experiments, and have been substantiated by the results of vaccination and serum treatment in human beings.

The evidences just summarized appear to warrant the conclusion that *L. icteroides* is the cause of yellow fever.

There is no reason for modification of any of the established measures of general prophylaxis or sanitary regulations now in force against yellow fever; specific prophylactic measures and serum treatment should be employed simultaneously with the antimosquito campaign and the proper symptomatic treatment of yellow fever.

A Note on the Treatment of Amebic Dysentery with Stovarsol. F. M. Johns and S. Chaille Jamison, J. Trop. Med. **28**:378 (Nov. 2) 1925.

Johns and Jamison report the results of treatment of twenty-seven cases of dysentery with stovarsol (oxyaminophenyl arsenic acid). These cases were followed with stool examination and proctoscopy. The drug was given by mouth, 0.25 Gm. three times a day for seven days. One course of treatment has sufficed in three subjects, who remained symptom free and ameba free for periods of seventy days and more. The remainder received a second similar course; sixteen of these have remained clinically cured and free of parasites; four have relapsed, these being cases of long standing. Few untoward effects were observed, headache in one case, a rash in two cases. The authors believe stovarsol to be a harmless remedy and as efficient as any other treatment.

Scott, Philadelphia.

Endocrines in Relation to Rheumatic Fever and Rheumatoid Arthritis. Llewellyn Jones Llewellyn, M. J. & Rec. **121**:670 (June 3) 1925.

Cardiac conditions in children often run an afebrile course, and considering that children of rheumatic stock are often hypothyroidic, the author believes that this thyroid deficiency is in some way responsible for the lack of fever in these cases. This afebrile character of these affections is also a feature more compatible with an anaphylactic than with an infective origin. Kolher of Berne states that severe rheumatism and heart trouble of unknown origin are due to hypothyroidism, and are cured by transplantation of thyroid tissue. The relationship between thyroid disorders and thyroid instability and rheumatic fever and rheumatoid arthritis are given in detail, also some interconnecting syndromes such as Raynaud's disease developing after some infective or toxic disorder, to be complicated weeks or months later by joint swellings.

The Present Status of the Control of Scarlet Fever. Ralph Oakley Clock, M. J. & Rec. **122**:159 (Aug. 5) 1925.

For many years the hemolytic streptococcus was suspected as the causal organism of scarlet fever, and accepted as this. During the last year, Dick and Dick distinguished the scarlet fever streptococcus by obtaining a soluble toxic substance in the filtrate after growing it in broth. This toxic substance gives a skin test, neutralizable with serum from a patient convalescent from scarlet fever. The author gives the Dick test in detail, and points out that it is complicated by the fact that the negative reaction does not always seem to indicate immunity. He suggests that two negative tests be obtained before considering the person immune to scarlet fever. The immunization dose is a multiple of the skin test dose, but the best dose for immunization has not yet been definitely established. Shultz and Charleston, in 1918, observed that when serum from a normal human being, or from one convalescent from scarlet fever, was injected into a patient suffering from acute scarlet fever, blanching

of the surrounding skin occurred and persisted, showing the serum in both cases contained antitoxin. Dochez was the first to produce an antitoxin horse serum against scarlet fever, and to use it in the treatment of the disease. The dose obviously depends on the severity of the attack. The same serum is used in the blanching test as a diagnostic measure, and also as a means of prophylaxis when both the Dick test and the throat culture of a contact are positive.

CONTROL OF MORBIDITY AND MORTALITY OF DIPHTHERIA. DWIGHT M. LEWIS, M. J. & Rec. **122**:199 (Aug.) 1925.

Lewis states that the control of morbidity and mortality of diphtheria is possible for two reasons; first, nasal carriers of diphtheria are evident to the eye, and second, measles is the chief cause of nasal diphtheria carriers. He says that diphtheria morbidity increases during and following epidemic measles; and that diphtheria mortality increases during the last half of the year when measles is epidemic during the first half, and that it extends into the first half of the following year. He cites the fact that a measles epidemic appeared in a certain district in New Haven in 1924, and that an examination for nasal diphtheria carriers in the city showed that over half the carriers for the whole city for that year were found in that district and that the majority of the carriers were found among those who had had measles.

Lewis gives statistics from other cities, which seem to show that diphtheria morbidity and mortality are greater following epidemics of measles.

MEDICOLEGAL AND SOCIOLOGIC ASPECTS OF EPIDEMIC ENCEPHALITIS. CHARLES S. POTTS, M. J. & Rec. **122**:335 (Sept. 16) 1925.

Epidemic encephalitis may occur without the typical symptoms of the acute stage and this stage is often unrecognized. The patients may develop physical and mental symptoms later that may bring them either into conflict with the law, or cause them to become public charges. Typical patients, apparently cured, may develop symptoms after several years of health. Sudden changes in personality and behavior, especially in children, should arouse suspicion that the condition may be a postencephalitic one. These children may be bright except for bad behavior. Criminal tendencies may be so caused. Physical symptoms may resemble those of syphilis, neurasthenia and hysteria, the mental especially resembling those of syphilis and other toxemias. Patients may hear and remember what is said in their presence while in the lethargic state, and may have periods of alertness and mental clearness. The question must be considered whether trauma can predispose to an attack or excite the sequelae in one who has had the disease.

WILLIAMSON, New Orleans.

THE SIGNIFICANCE OF THE BLOOD PICTURE FOR THE DIFFERENTIAL DIAGNOSIS OF DIFFERENT FORMS OF MENINGITIS IN INFANTS AND IN CHILDREN. F. HEISZEN, Med. Klin. **21**:1301, 1925.

In infants and children, the qualitative blood picture makes the differential diagnosis between tuberculous and purulent meningitis possible.

The blood picture in purulent meningitis is characterized by the appearance of numerous pathologic leukocytes and a marked shifting to the left. In the beginning there are only a few monocytes.

In tuberculous meningitis the cells are from the beginning of normal structure and remain so (no toxic forms, no shifting to the left). There are a great number of monocytes.

The different forms of purulent meningitis present the same blood picture. The blood picture cannot be used for differential diagnosis from other infectious diseases. It does not help in the differentiation of meningitis from meningismus, meningitis serosa or encephalitis.

HEMATOLOGIC STUDIES IN SCARLET FEVER. H. BIX, Med. Klin. **21**:1728, 1925.

The blood pictures in uncomplicated cases of scarlet fever show a great similarity, chiefly in the time from the climax to the fading out of the exanthem. The eosinophils reach their highest number usually on the sixth day; they drop just before the beginning of the convalescence and rise again during this. Therefore, we can distinguish between the first increase of the eosinophils as the scarlatina eosinophilia proper and the second increase during the convalescence. The scarlatina eosinophilia proper is in close connection with the exanthem. As to the structure of the nucleus of the white blood cells—independent of the gravity of the case—there are two different forms of scarlet fever, the one with shifting to the left the other without. The scarlatina virus does not cause any shifting but only a toxic damaging of the cells. The shifting to the left is due to mixed infection. Of ten grave cases of scarlet fever, only the ones with shifting to the left in absence of cell damaging have reacted to treatment with serum and electrocollargol.

ZENTAY, St. Louis.

SCARLET FEVER: WITH SPECIAL REFERENCE TO SUSCEPTIBILITY AS DETERMINED BY THE DICK INTRACUTANEOUS TEST. W. A. BROWN, Brit. J. Child. Dis. **22**:171 (July-Sept.) 1925.

The test demonstrates that there are but a small number of susceptible subjects under the age of 1 year and again over the age of 10; which is in accordance with the incidence of the disease as shown by hospital records. An abnormally high percentage (62 per cent.) was found between the first and second year.

In patients with acute scarlet fever tested during the first five days of illness, thirty showed eight positive reactions (26.6 per cent.), as against 100 per cent. positive results of Zingher and 61.1 per cent. positive results of Kerr. Retests done on the fourteenth day of disease were all negative.

A series of sixty convalescent scarlet fever patients tested between the seventh and 120th day showed six positive reactions. Five of these cases were clinically doubtful scarlet fever.

The author used two dilutions of toxin, 1:6,000 and 1:1,000, and concluded that in the second series (1:1,000) the toxin was sufficiently diluted.

He, furthermore, did not confirm the observation of Zingher that an area of pallor appears at the site of the previous injection in a positive reactor who contracts the disease.

The well recognized fact that an attack of diphtheria increases the patient's susceptibility to scarlet fever is confirmed by this test.

LANGMANN, New York.

ETIOLOGY OF CHRONIC PYURIA. WOLFGANG COURTIN, Monatschr. f. Kinderh. **31**:24, 1925.

The writer describes three cases of chronic pyuria in children, in whom the etiologic factor was a malformation of the bladder. In only two of these was the condition diagnosed during life. Roentgenograms and a diagram are shown.

GERSTLEY, Chicago.

PROTEUS MENINGITIS IN INFANCY. BISCHOFF and BREKENFELD, Ztschr. f. Kinderh. **39**:421 (May 22) 1925.

To the three reported cases of proteus vulgare meningitis is added a fourth one, with complete pathologic and bacteriologic data. There was probably a cerebral injury at birth followed by a chronic leptomeningitis, and on this was superimposed an infection with proteus, secondary to an infection in the intestines. The authors believe that this case bears out the contention of Klieneberger, of Metschnikoff and of Zeiss that more consideration should be given to the proteus vulgare bacillus as a pathologic organism.

EFFECT OF BEEF SERUM ON MEASLES. NOBEL and SCHÖNBERGER, Ztschr. f. Kinderh. **39**:434 (May 22) 1925.

Those with scarlet fever infected with diphtheria having been reported as aborted by the use of diphtheria antitoxin, led the authors to try the effect of beef serum on measles in the beginning. Beef serum was used because it was reported to cause serum sickness rarely. Transient heart weakness developed in two subjects, and although some cases of measles seemed to be shortened, others developed typically. Nor was the hope fulfilled that no serum sickness would result. Beef serum was, therefore, considered not only inefficient but unsafe.

EMERSON, Boston.

Chronic Infections

TREATMENT OF VISCERAL SYPHILIS WITH BISMUTH. J. H. MUSSER, Am. J. Syph. **9**:589 (Oct.) 1925.

The author reviews the status of the use of bismuth. Bismuth is indicated in those conditions in which the arsenicals are contraindicated, that is, in cardiovascular syphilis, nephritis, etc., and in cerebrospinal syphilis. It is a drug with marked spirochetocidal powers and low toxicity.

THE BISMUTH TREATMENT OF SYPHILIS. IRWIN C. SUTTON, Am. J. Syph. **9**:600 (Oct.) 1925.

The author reviews the history of the use of bismuth. It was first used by Balzar as an antisyphilitic remedy in 1889. Its use was renewed and popularized by Sazerac and Levaditi in 1921. It is largely excreted by way of the kidneys but also in the large intestine, saliva and bile. He states that the spirocheticidal action is very prompt, as evidenced by the Herxheimer reaction and the healing of visible lesions. The action on the tertiary lesions is quite marked, especially in cerebrospinal syphilis. Its use is also admissible in aortic aneurysm and nephritis when arsenicals are contraindicated. The accidents with its use are very few, the chief of which is stomatitis, and with

adequate prophylactic dental care this accident seldom occurs. When it does develop, it yields readily to local measures and to the use of sodium thiosulphate.

Occasionally, one sees cutaneous lesions, erythema, urticaria and rarely exfoliative dermatitis. The drug is recommended as an antisyphilitic remedy.

BILATERAL CHARCOT HIP JOINTS. REPORT OF THREE CASES. JAMES L. GREENE and FRANCIS J. SCULLY, Am. J. Syph. **9**:704 (Oct.) 1925.

In discussing Charcot joints, the author points out that they do occur in juvenile tabes of congenital syphilis. The usual age of onset is about 14 years.

McBRIDE, Iowa City.

THE WASSERMANN TEST. XV. THE EFFECT OF BISMUTH ON THE WASSERMANN REACTION IN PATIENTS UNRESPONSIVE TO ARSPHENAMIN. DAVID L. BELDING, Arch. Dermat. & Syph. **12**:334 (Sept.) 1925.

In review, it is stated that 0.001 Gm. of metallic bismuth per kilogram of body weight is the average therapeutic dose for man. This dose is one hundredth (Sazerac and Levaditi), one hundredth and twenty-fifth (Klauder) and one fiftieth (Hopkins) of the lethal dose for rabbits. The sterilizing dose is from one fourth to one fifth (Sazerac-Klauder) of the maximum tolerated dose, or twenty-five times the average dose for man. The average dose for man produces definite curative effects in rabbits. The chief objection to bismuth appears to be the narrow range between the toxic and the sterilizing dose.

The author adopted as a standard dose 0.002 Gm. bismuth per kilogram for each of ten weekly injections. He gave the adults slightly less than this dose. He reports on the treatment of forty-one adults and eight children who were "Wassermann-fast."

Of the injections of potassium bismuth tartrate, 10 per cent gave moderate or severe local reaction. Slight induration which did not materially trouble the patient was frequent. A sterile abscess developed in one patient. Only two patients gave reactions sufficiently severe to interfere with the continuance of treatment. A few patients showed enteritis, gingivitis, neuritis and general debility.

Of the forty-nine patients, nineteen showed no reduction in the Wassermann reaction, sixteen showed moderate and fourteen marked reduction. Most of the reduction was obtained by the fourth week after the termination of treatment.

OBSERVATIONS ON THE SIGMA REACTION FOR SYPHILIS. H. EVERETT SMILEY, Arch. Dermat. & Syph. **12**:345 (Sept.) 1925.

The Sigma reaction is a flocculation test devised by Dreyer and Ward as a modification of the Sachs-Georgi test. Results are expressed quantitatively. The author presents evidence to show that the Sigma reaction offers a reliable index in following the effect of a course of treatment for syphilis. The validity of the reaction is not affected by treatment as is the Wassermann reaction.

CURATIVE EFFECT OF BISMUTH COMPOUNDS IN EXPERIMENTAL RABBIT SYPHILIS. GEORGE W. RAIZISS and M. SEVERAC, Arch. Dermat. & Syph. **12**:661 (Nov.) 1925.

On the basis of experimental data presented, the authors conclude that bismuth compounds are powerful enough to cause complete eradication of infection in experimental rabbit syphilis. It was found that potassium bismuth

tartrate and bismuth compounds in general are much less toxic intramuscularly than intravenously. Bismuth compounds are distinctly superior to mercury, but have a lower chemotherapeutic index than the arshphenamines. Arsphenamine derivatives remain the basic remedies in the treatment of syphilis, bismuth compounds taking the next place.

THE BLOOD WASSERMANN REACTION IN EXPERIMENTAL RABBIT SYPHILIS. G. E. WAKERLIN and P. H. CARROLL, Arch. Dermat. & Syph. **12**:670 (Nov.) 1925.

The validity of the Wassermann reaction in rabbits is established. A parallelism is shown between the serologic and clinical manifestations of syphilis. When the clinical signs disappeared, the Wassermann reaction became negative. When a clinical relapse occurred, the Wassermann reaction frequently became positive again. The Wassermann reaction did not become positive when keratitis was the only generalized manifestation. When alcohol was ingested, the degree of positiveness was decreased but the Wassermann reaction did not become negative. Attempts to provoke a positive reaction in rabbits with latent syphilis were unsuccessful. The Wassermann test is a measure of tissue reaction to spirochetal influence, and bears no relation to the question of sterilization in regard to the spirochete.

FLUMERIN IN OPHTHALMOLOGIC COMPLICATIONS OF SYPHILIS. JOHN F. HOGAN and J. CLAGETT ROBERTSON, Arch. Dermat. & Syph. **12**:700 (Nov.) 1925.

In the routine use of flumerin in a syphilitic clinic, it was accidentally observed that flumerin is of great value in syphilis of the eye, particularly when it is given intravenously. No other remedy has shown a beneficial effect as quickly.

JEANS, Iowa City.

RÔLE OF NONGRANULAR BLOOD LEUKOCYTES IN THE FORMATION OF THE TUBERCLE. ALEXANDER A. MAXIMOW, J. Infect. Dis. **37**:418 (Nov.) 1925.

The study of in vitro cultures of various tissues, and of blood leukocytes inoculated with tubercle bacilli, shows that the epitheloid and giant cells of the tuberculous lesions have the same double origin as the polyblasts or mononuclear exudate cells in common or purulent inflammation. They arise partly from the local fixed elements and partly from the migrated (or local, if available), nongranulated, that is, lymphoid white blood corpuscles — both monocytes and lymphocytes. According to the tissue and to the special circumstances of the case, the relative number of the epithelioid cells of the two origins may vary. If there are no leukocytes available, the epithelioid cells will be of purely local, histiocytic origin. If, on the contrary, in cultures of leukocytes or, for instance, in the early stages of tuberculosis, following the intravenous injection of bacilli, only leukocytes are available near the bacilli, the primary tubercles will consist only of transformed lymphoid cells, lymphocytes and monocytes. No sharp discrimination between monocytes and lymphocytes could be made regarding their rôle in the formation of the tubercle. The monocytes respond more promptly to the stimulus and, being larger and better prepared for the defense reaction, sooner reach the fully developed epithelioid stage. The lymphocytes are slower, but nevertheless they follow in the same way, and sooner or later join the monocytes in their transformation into epithelioid cells.

KENNEDY, Rochester, Minn.

Internal Diseases

NONENDEMIC ENLAGEMENT OF THE THYROID GLAND IN JUVENILES. H. FINKELSTEIN, Pediatria **3**:1 (June) 1925.

This subject is surveyed because of its lack of treatment in most pediatric textbooks. Material for basic study must necessarily come from nongoitrous areas, in which the noxious agent responsible for endemic goiter is missing. Observations of Schlesinger and Francks compared favorably with those of the author.

The incidence, the degrees and types of nonendemic enlargements and the occurrence of toxic symptoms are mentioned. Physiologic growth, hereditary and familial influences, relation of sexual growth and iodine insufficiency are given etiologic significance.

The author states that the chief difference between nonendemic thyroid enlargements and the endemic form must be sought in the difference in origin, which will at the same time explain the difference in incidence. A further difference is noted by grouping the cases according to social standing. The nonendemic form is most commonly encountered in the higher intellectual classes, while the opposite has been found true in the endemic form.

The well known results of iodine therapy in the endemic form cannot be applied without further trouble to nonendemic enlargements. Owing to the comparative innocence of the latter type, no specific therapy is indicated. Nothing in the literature has been found regarding the usefulness of iodine; Schlesinger has used a brand of iodine, with good results, and Pototzky recommends ovarian substances.

BUHRMANN, Chicago.

THE PATHOGENESIS OF THE ANEMIA INFANTUM PSEUDOLEUKEMICA JAKSCH. R. FISCHL, Med. Klin. **21**:1077, 1925.

The author summarizes his experiences with this form of infantile anemia and also the data in the literature. He comes to the conclusion that the so-called v. Jaksch anemia of infants is not a primary blood disease, but it is one of the secondary anemias due chiefly to the rachitic affection of the bone marrow.

ZENTAY, St. Louis.

Nervous Diseases

BREECH DELIVERY AND ITS POSSIBLE RELATION TO INJURY OF THE SPINAL CORD WITH SPECIAL REFERENCE TO INFANTILE PARAPLEGIA. F. R. FORD, Arch. Neurol. & Psychiat. **14**:742, 1925.

Ford reports a series of six cases of paraplegia following breech delivery or version and extraction, in all of which a history of protracted and forced labor was obtained. The infants varied in age from 3 days to 18 months. Five of them were over 3 months of age and were still living. The single fatal case died on the third day.

In all cases, the lesion was high in the thoracic region, with the exception of the fatal case in which the lesion was in the lower cervical cord. Clinically, the condition was characterized by paralysis below the midthoracic region with disturbance of sensation. The tendon reflexes for the most part were lively or hyperactive. Five cases showed the flexion reflex and in two cases "mass" reflexes were obtained. Slight flaccidity was present, but atrophy and trophic disturbances were insignificant. Roentgen-ray examination revealed no sign of injury to the spinal column.

The postmortem examination on the one fatal case showed a rupture of the spinal dura, with stretching and softening of the spinal cord in the region of the eighth cervical and first dorsal segments. Sections of the cord revealed marked infiltration with blood.

The fact that the tendon reflexes were active bears out the experimental findings in young animals in which the cord has been severed, and in which the reflexes are more active and appear after a shorter latent period than in older animals with cross section of the cord.

The fact that five of these infants were seen during two years of practice tends to show the relative frequency of the condition.

BEHAVIOR DISORDERS OF CHILDREN. PSYCHOLOGIC EXAMINATION. BERT I. BEVERLY, Arch. Neurol. & Psychiat. **14**:769 (Dec.) 1925.

Beverly discusses the importance of the psychologic examination as a part of every mental examination, and points out what information such an examination may contribute to the better understanding of the child. The examination can determine the level of intelligence and the intelligence quotient which can be used as an accurate index to the rate of development, as well as the extent of the development. It can point out special abilities as well as special defects, and other individual characteristics of the child's mental process. To a certain extent it can foretell the educational ability and how far and how fast learning can be acquired.

BEHAVIOR DISODERS IN CHILDREN. MEDICAL ASPECTS. HERMAN M. ADLER, Arch. Neurol. & Psychiat. **14**:779 (Dec.) 1925.

Adler points out that the struggle for survival is the underlying characteristic of living organisms. Man lives in an environment that he himself has modified, but changes in environment are slow and do not keep up with the changing responses within the organism. The ability of persons to adjust themselves easily to their environment varies, and when adjustment cannot be made easily, behavior disorders result. When the behavior of an individual markedly deviates from that of the members of his own group, the cause should be looked for in the individual rather than in the environment. The writer points out that the explanation of the behavior disorder may lie in the subconscious responses or in pathologic conditions that weaken the individual, such as malnutrition, hereditary factors, endocrine disturbances, or diseases of the brain.

BEHAVIOR DISORDERS OF CHILDREN. PSYCHANALYTIC STUDIES. DAVID M. LEVY, Arch. Neurol. & Psychiat. **14**:786 (Dec.) 1925.

Levy discusses the psychanalytic aspect of behavior disorders in children, and points out that it should be a part of the examination. When combined with the results of other types of examinations it may be of great value, whereas taken alone it might fall short in explaining the misconduct. He gives as examples two cases of abnormal reactions which could be explained by psychanalytic study, but in which further investigation revealed the presence of organic factors which were either basic or related to the psychical disturbance. The writer points out clearly the psychic characteristics of the normal adolescent masturbation, with instances showing abnormal psychic accompaniments which need psychanalytic study.

AVERY, Chicago.

ENCEPHALITIS LETHARGICA. W. M. CROFTON, M. J. & Rec. **122**:331 (Sept. 16) 1925.

The manifestations of encephalitis lethargica depend on the position, extent and severity of the lesions in the central nervous system; symptoms varying from a slight central irritation to an acute meningo-encephalitis. The symptoms may entirely clear up, or so many brain cells may be destroyed that the patient may be left in a state of helpless palsy. The author states the etiology of the disease is hopelessly confused, authority asserting that nothing whatever is known of the disease, but he himself believes we should look for the influenza bacillus as the cause and gives experiments to prove this statement. Diagnosis is made by lumbar puncture. The author treats his patients with a potent antigen of the influenza bacillus, and in some cases gets remarkable results.

One profoundly lethargic patient, after one millon doses of this antigen, was sitting up and talking sensibly within two hours. He gives one million to four million doses at intervals, depending on reaction obtained in acute cases. Larger doses are required when the condition has lasted for a long time. The author then reports a few cases treated in this way.

WILLIAMSON, New Orleans.

PSYCHOLOGIC TESTS IN THE DIAGNOSIS OF MENTAL DEFICIENCY. G. M. WILLSON, J. Psycho-Asthenics **30**:84 (June) 1924-1925.

Tests for mental deficiency may be classified as follows:

1. Those involving chiefly verbal material—the Stanford Binet test—of value especially in testing school ability.

2. Group verbal tests, such as the army alpha tests, the national intelligence tests. These employ arithmetic problems, sentences with words omitted which the examinee is to fill in; analogies in which one word must be chosen from a list of possible ones, that is, hat is to head as shoe is to (stocking, leather, slipper, foot). These are valuable to pick out extreme cases for more careful testing.

3. Nonverbal tests, designed to be given with pantomime directions. (*a*) Individual nonverbal tests, such as the army designs test, measures ability to remember and to draw simple designs after the examinee has been allowed to look at them for ten seconds. The Porteus maze tests presents a series of increasingly complicated line patterns, through which a pencil is to be traced without entering any blind alleys. (*b*) Group nonverbal test: These tests utilize pictures with absurdities which are to be discovered and marked; pictures with omissions to be indicated or inserted.

4. Aptitude tests. Most special tests for vocational guidance purposes have little application to the feebleminded. Verbal and nonverbal intelligence tests usually sufficiently point the way to the work which these individuals must do.

5. The questionnaire for testing personality has only a limited use with feebleminded individuals.

EHRMANN, Chicago.

Diseases of the Eye

AGE INCIDENCE OF CONJUNCTIVITIS ECZEMATOSA AND OTHER EXTERNAL EYE DISEASES. KRASSO, Ztschr. f. Kinderh. **39**:448 (May 22) 1925.

The author sums up by Pirquet's statistical method, the incidence of external eye diseases, according to age, a method which according to Pirquet brings

out the interdependence of various diseases. Conjunctivitis eczematosa and phlyctenular keratitis show a complete unanimity in age distribution, ascent of 2 years, apex at 4 to 14, the highest apex at 15, and after that a quick fall. Hordeolum and chalazion are different from these diseases in age distribution, but very similar one to another. Their ascent appears between 10 and 20 years, apex at 22 years, and a gradual fall after that. According to Pirquet's conception, all four of these diseases belong to the tuberculous group. All four have the same apex as the youthful form of tertiary tuberculosis, and all disappear gradually after the twenty-second year. It is true of conjunctivitis eczematosa and phlyctenular keratitis but not of hordeolum and chalazion that there is an apex corresponding to the apex of secondary tuberculosis.

EMERSON, Boston.

Diseases of the Ear, Nose and Throat

ROENTGEN-RAY TREATMENT OF TONSILS AND ADENOIDS. P. B. MACCREADY, Am. J. Roentgenol. **13**:425 (May) 1925.

Roentgen-ray treatment causes a definite shrinkage of tonsil lymphoid tissue and less definitely of adenoids, because these are not directly irradiated. Roentgen ray has no effect on local sepsis in the tonsils and adenoids, but it offers ideal treatment for shrinking lymphoid tissue in hyperplasia, but does not replace operation in cases of local sepsis.

ROENTGEN DIAGNOSIS OF NONOPAQUE FOREIGN BODIES IN THE TRACHEA. WILLIS F. MANGES, Am. J. Roentgenol. **13**:429 (May) 1925.

Foreign body aspiration is frequent in childhood, and spontaneous expulsion occurs in only 2 per cent of cases, according to Chevalier Jackson. Lung abscess quickly follows if the foreign body is not removed and especially after nonopaque bodies, which are usually vegetable or organic. Roentgen diagnosis of nonopaque bodies in the trachea or bronchi is almost always possible at the first examination. Repeated examination detects the movable body by some variation in the function of the lungs or the heart and diaphragm relation. The usual pathology is either (1) obstructive emphysema, (2) atelectasis, (3) drowned lung, (4) abscess or a combination of two or more. The roentgen signs of unilateral obstructive emphysema are: (1) increased transparency of the affected lung, (2) depression and partial fixation of the diaphragm on the affected side, (3) displacement of the heart and mediastinal structures away from the affected side, and (4) increased excursion of the diaphragm on the unaffected side, due to compensatory emphysema. (The first three are most noticeable at the end of expiration.) Short exposure of one thirtieth to one fifteenth of a second of a moderately short spark gap at 36 inches with an intensifying screen and a rapidly acting time switch, to produce identical exposures, are advocated. Plates and references are given.

STULIK, Chicago.

THE SIZE OF THE TONSILS IN CHILDHOOD. SCHÖNBERGER, Ztschr. f. Kinderh. **39**:367 (May 22) 1925.

In a study of 5,670 cases in Pirquet's clinic, hypertrophy of the tonsils was first recognized in the second year of life, its incidence reached the maximum in the fourth year, and a second maximum in the tenth year, then diminished

in frequency up to the eighteenth year, so that almost no enlargement persisted; operative interference played little part in the incidence. The most important fact was that the percentages of enlarged tonsils, slight or great, fell from 75 per cent in the tenth year to 25 per cent in the eighteenth year.

EMERSON, Boston.

Diseases of the Skin

ANGIOMA CAVERNOSUM. CHESTER N. FRAZIER, Arch. Dermat. & Syph. **12**:506 (Oct.) 1925.

A large angioma of the face in a young infant had completely disappeared in eight months, after a single application of radium.

JEANS, Iowa City.

Surgery and Orthopedics

IS IRRADIATION A SATISFACTORY TREATMENT FOR SUBSTERNAL THYROID? G. W. GRIER, Am. J. Roentgenol. **13**:327 (April) 1925.

Surgery is regarded as the only treatment by some authors. Irradiation is regarded as dangerous by some, because of the frequency of adenoma and the danger of secondary hypothyroidism through the effect on normal gland. The intrathoracic goiters are mostly adenomatous and a few are either cystic, colloid or exophthalmic. Only the adenomatous and exophthalmic are reduced by radiation. The question of fibrosis with relation to secondary operation and hemorrhage is debatable. Surgery is the treatment of choice, and, if not, irradiation offers a probability of relief from symptoms in a majority of cases.

METASTATIC MANIFESTATIONS OF HYPERNEPHROMA IN BONE. RICHARD DRESSER, Am. J. Roentgenol. **13**:342 (April) 1925.

The literature reveals forty-three cases, with an average age incidence of 40 to 60 years, but the disease may occur in childhood. The bones involved were the femur, vertebrae, ribs, skull, clavicle, pelvis, humerus, scapula, jaw, tibia and metacarpus. The diagnostic points: The lesion is purely destructive and involves the soft tissue. Lesions conform to anatomic distribution of red bone marrow and are rarely distal to the humerus and femur. There is no new bone formation except when complicated by healing fracture. (One case of osteoplastic tumor of the occiput reported.) Clinically, pulsation similar to an expansile aneurysm often occurs. In two cases, a definite reduction with alleviation of symptoms followed marked erythema doses of deep therapy. Favorable prognosis after radical excision of solitary metastasis and nephrectomy is cited.

STULIK, Chicago.

PREVENTIVE ORTHOPEDICS. REGINALD H. SAYRE, M. J. & Rec. **122**:599 (Nov. 18) 1925.

Orthopedics is the art of preventing and correcting deformities in children. In almost every ailment, nature gives us warnings before trouble comes, and if we heed these, many maladies can be prevented; this is especially true in orthopedic surgery. Rickets is one of the most prevalent causes of deformities. There are early and minor symptoms of this disease which should be watched for and if found, the disease should be treated before deformities develop.

Improper posture is a frequent cause of orthopedic deformities. The majority of people stand with the back too much swayed, the abdomen protruding and the chest caved in, the neck being poked too much forward. They should be shown before a mirror how to stand and then they should consciously hold themselves in this position for one minute every hour till the correct position is maintained. A slight deviation from normal in growing children may be the precursor of deformities. Inequalities in length of legs should be corrected by arranging the shoe to prevent curvatures of the spine. If a child complains frequently of stomach ache, he may have spinal tuberculosis. "Growing pains" may be caused from inflammation of joints. Pain in the foot or the knee may be beginning of tuberculosis of the hip. These things should be treated before deformities begin.

DISCUSSION ON THE DIFFERENTIAL DIAGNOSIS OF NONTUBERCULOUS COXITIS IN CHILDREN AND ADOLESCENTS. ALLAN H. TODD, Proc. Roy. Soc. Med. **27:** 231 (Aug.) 1925.

A few years ago, practically all painful affections of the hip-joint occurring in young subjects were assumed to be tuberculous, but it was obvious from the course of the disease in some of these cases that they were not tuberculous. Nowadays, certain well defined conditions have been clearly eliminated from this group. The author divides these conditions into five main groups.

1. Traumatic cases (*a*), simple contusions of the hip which heal spontaneously. (*b*), When the articular cartilage has been bruised, these cases clear up in a few days with rest in bed. (*c*), Justa-epiphyseal strain.

2. Infective cases which follow directly from febrile condition, the commonest being measles.

3. Coxa vara, this condition is well recognized.

4. Coxitis of secondary onset. These cases are generally secondary to operations in septic areas.

5. Arthritis deformans juvenilis. In this form, there is gradual destruction of the articular cartilage of the head of the femur leading to disablement and ankylosis.

6. Miscellaneous cases, when the diagnosis is usually easy. 1. Hemophilia leads to recurrent attacks of pain and limitation of movement. 2. In scurvy, there are the usual signs of the disease to help one. 3. Intestinal pseudocoxitis, a peculiar condition occurring in the constipated child.

The author then discusses the diagnosis. He considers the injection of tuberculin for diagnostic purposes dangerous.

WILLIAMSON, New Orleans.

Miscellaneous

INFANT MORTALITY AND SURVIVAL OF THE FITTEST. CHARLES HERRMAN, Scientific Monthly **22**:25, 1926.

This article deals with the question of factors and conditions affecting infant mortality. Among the conclusions are the following:

The two seemingly opposed views with regard to the advisability of reducing the infant mortality are not incompatible. There are two distinct groups of causes of deaths in infants; one is due to defects in the germ plasm and destroys the weak; the other is largely accidental, affects the strong as well as the weak and is, to a great extent, preventable. The reduction in infant mortality

has been almost entirely in the latter group. A high infant mortality sacrifices the unfortunate as well as the unfit. Natural selection is still operative. There has been no reduction in the number of miscarriages, stillbirths or deaths due to congenital debility. There has been little reduction in deaths in infants due to infectious and respiratory diseases because these have been largely beyond our control.

EHRMANN, Chicago.

THE EFFECTS OF VARIOUS BATHS ON INFANTS. A. LARUSSO, Clin. Pediat. **7**:405-424, 1925.

The warm or tepid water baths alter the cutaneous circulation very perceptibly. They stimulate the heat regulating and emunctory properties of the skin, as shown by an increase in the "perspiratio insensibilis."

Air baths also increase the thermoregulatory powers and the "perspiratio insensibilis." They are of value in the stimulation of body vigor.

Sun baths activate the peripheral circulation and enhance the excretory function of the skin. This is especially marked in older children.

ZAMBARANO, Northville, Mich.

TEETH AND TEETHING. H. KLEINSCHMIDT, Pediatria **3**:7 (June) 1925.

The anomalies of the jaw and palate are mentioned as features of interest in the new-born. Heredity, thumb sucking and nasal obstruction are given etiologic significance.

Rickets is the factor of greatest importance in delayed dentition, although in myxedema the delay is more pronounced. Family peculiarities can also be observed, and it is incorrect to assume a metabolic disorder in every case of delayed dentition. Some hereditary peculiarity is now thought to be the important factor in dentitio praecox.

The relationship of teething to disorders of childhood is one of coincidence and the reasons for their association is given. Anomalies of the teeth due to rickets, syphilis and malnutrition are described and dental caries and its etiology are considered.

A FEW IMPORTANT PEDIATRIC QUESTIONS. J. HUSLER, Pediatria **3**:12 (June) 1925.

Many of the recent important researches in pediatrics, for example blood transfusion in anemia, are of greater value in hospitals than in private practice. Important progress, however, has been made in the treatment of rickets.

Due to the disagreement on the part of physicians as to what constitutes a diagnosis of rickets, statements concerning the incidence disagree remarkably.

The use of cod liver oil has given practical prophylactic and therapeutic results. Besides cod liver oil, irradiation treatment has proved most beneficial. Pluriglandular substances in the hands of some observers have also given good results. Recent suggestions are massage and gymnastics of the infant, but this has been used for many years in Germany. The basis for each of the various methods of treatment is given.

The discussion on the prophylactic inoculation against diphtheria gives the theory, method of administration and occurrence of reactions. Fever is practically the only contraindication for its administration, and this is only temporary.

The need for inoculation is greatest in older infants, that is, those from 10 months on, and in small children, as susceptibility is greatest at this age and infections are more severe.

The Schick test shows whether or not there are antibodies present in the body, but its usefulness is decreased by the unstableness of the material used.

BUHRMANN, Chicago.

A SIMPLE METHOD FOR THE TREATMENT OF OXYURIASIS. F. H. LORENTZ, Med. Klin. **21**:95, 1925.

The usual methods of treatment did not bring any results in the hands of the author. Following the reasoning that the worms develop and multiply in the small remnants of stool remaining around the anus after each bowel movement, he tried simple, thorough washing of the anus with water after every bowel movement. The results were striking. In from eight to fourteen days the worms disappeared without any recurrence.

THE RÔLE OF THE EPINEPHRIN AND INSULIN SYSTEM IN INFANTILE PATHOLOGY. J. DUZAR, Orvosi hetil. **69**:608, 1925.

There are two methods of testing the epinephrin and insulin system of infants, namely, changes in the blood sugar after injection of the hormones, and measuring the changes in volume of the liver by the use of roentgen rays. Infants with alimentary intoxication give a high and protracted increase in the level of blood sugar on intravenous injection of epinephrin; the same infants show a slight and short decrease on injection of insulin. Infants with decomposition react with a slight hyperglycemia to epinephrin, followed by a second phase of deep depression. In toxic pneumonias the blood sugar curve on epinephrin injection may be entirely reversed, showing only the second phase.

On epinephrin the volume of the liver decreases, on insulin it increases. It decreases on hypertonic, increases on hypotonic glucose solutions.

Treatment of alimentary intoxication with insulin is very reliable if combined with intravenous injection of hypotonic glucose solutions. Very good results have been obtained in toxic pneumonias, with combined intravenous injection of epinephrin and hypertonic glucose solutions.

ZENTAY, St. Louis.

THE BODY WEIGHT OF INFANTS. J. AXEL HÖJER, Acta Pediat. **5**:59, 1925.

This is a statistical study of children from working class families in a suburb of Stockholm. The relation between age and weight has been studied in various groups of children. Weight curves for breast fed and artificially fed infants agree well with those obtained in other countries. In normal children, the birth weight (averaging 7.1 pounds) is doubled in 164 days. In small children the birth weight (averaging 5.3 pounds) is doubled in 112 days. All groups of children showed a minimum rate of gain at about 6 months of age. The more rapid gain after this can be attributed to supplementary food. Children with "physiologic craniotabes" show weight curves identical with those of children with hard skulls. This confirms the author in his belief that this entity bears no relation to rickets.

HOLT, Baltimore.

NONSPECIFIC PROTEIN THERAPY. N. R. CHRISTOFFERSEN and E. POLACK, Ugesk. f. Læger **37**:791, 1925.

The authors tabulate the findings in forty-three cases of various conditions treated with subcutaneous injections of different proteins. It appears that milk

injections are the most effective, and that the best results are attained in acute rheumatism and acute hepatitis. No benefit is noticed in chronic rheumatism, and the treatment is contraindicated in cases in which there is a tuberculous process.

The curative action of protein injection is considered to be due to the generalized reaction which stimulates the formation of antibodies and increases the transport of these as well as leukocytes to the focus of infection.

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ISAAC A. ABT, M.D., *in the Chair*

ENDOCARDITIS IN CHILD WITH CONGENITAL HEART DEFECT. Presented by DR. STANLEY GIBSON.

The patient, a girl, aged 12 years, presented the classical picture of congenital heart disease, with the marked cyanosis seen only in these cases. The child first came under observation at St. Luke's Hospital when she was 18 months old, and at that time had typical lobar pneumonia. The congenital heart defect was discovered at that time, and a faint basal systolic murmur was present. She recovered from the pneumonia without any embarrassment and I have seen her many times since. The interesting feature has been that in spite of the high grade cyanosis and the fact that the child was so crippled that she was able to get around only part of the time, practically no murmur was heard. If one listened carefully, a sharp, scratching murmur could be heard over the second left interspace. Last spring, during one of her trips to the dispensary, she was admitted to the hospital, for at that time she complained of pain in the legs and the arms. One of my colleagues thought it was rheumatism, but I was not convinced of this because many of the patients with heart trouble have intermittent obscure pains. There was no redness, tenderness or pain in the joints. While in the hospital she developed a severe tonsillitis, with elevation of temperature to 102 and 103 F., and at that time had acute pains in the joints. She remained in the hospital for two months, and during that period developed endocarditis with a definite systolic murmur at the apex, which she had not had before. Coincident with this a different type of systolic murmur developed over the second interspace, which became much louder than previously.

When the patient was returned to the convalescent home, the physician in charge, the matron and all the nurses and interns remarked that they hardly recognized her. The cyanosis was distinctly less following the development of the acquired heart condition.

I know it is rather hazardous to make a diagnosis of acquired heart disease on top of congenital heart disease. I think none of us are absolutely sure of the murmurs which may occur in congenital heart disease, but in this case the murmurs developed while the child was in the hospital, and probably the dilatation of the heart due to the acquired heart disease led to the better admixture of the blood and the improvement of the cyanosis. The red blood count, taken a number of times at Northwestern University Medical School prior to the development of the endocarditis, was always between 5,000,000 and 6,000,000, usually the latter, and it is now between 4,000,000 and 5,000,000.

As to the frequency with which acquired heart disease occurs in patients with congenital heart disease, I think there are not many records. Gilbert thinks it develops more frequently in such cases than in children free from congenital heart disease.

THE ROENTGEN-RAY TREATMENT OF PERTUSSIS. Presented by DR. R. A. Black.

Seven hundred and eighty cases of whooping cough have been treated by this method. All doubtful cases and all cases in which I had not complete record were eliminated, and now only those that were definitely whooping, or were coughing in a family with other children who were whooping, are reported. Four hundred cases, in which 228 patients, or 57 per cent, were not benefited are reported. In 90 cases, or 22 per cent, the benefit was doubtful. By doubtful, cases are meant in which the mother came in quite enthusiastically, and thought the child was much better; the cough was softer but almost as frequent, but clinically much improvement was not found. Eighty-seven patients were definitely benefited. Of the 228 unimproved patients, 85 per cent were treated during the first to the third week, and 15 per cent treated after that period. Of the doubtful improved patients, 95 per cent were treated during the fourth week. Practically all who were definitely benefited were treated during the third or fourth week of the disease. The time the treatment began was of interest. Those treated during the first and second week showed 69 per cent, no improvement; 33 per cent, doubtful improvement; 8 per cent, positive benefit. Those treated during the second and third week showed 40 per cent, no improvement; 47 per cent, doubtful improvement; 13 per cent, positive benefit. Those treated during the third and fourth week showed 80 per cent positive improvement.

In the entire series it cannot be said that it shortened the course of the disease in any way. They could be grouped as follows: Patients who coughed for four and five weeks; those who coughed for six and seven weeks, and those who coughed for eight and nine weeks. The patients who coughed between four and five weeks constituted 16 per cent of the total number, and roentgen-ray therapy was of positive benefit in 65 per cent of this group. The second group showed the treatment negative in 45 per cent, doubtful in 45 per cent and positive in 10 per cent. The third group, those who coughed for eight or nine weeks, of which 75 per cent were treated in the first week of the disease, 15 per cent in the second, and 10 per cent in the third, the treatment was negative in 95 per cent, doubtful in 5 per cent and positive in none.

In reviewing the work, it is concluded that the roentgen ray has no effect whatever on the whooping cough germ; that the ideal time in which to give the treatment is between the third and fourth week. This is the time the patients normally should begin to improve, but there would seem to be a marked hastening in the improvement when the roentgen ray is used, many of the children never coughing or vomiting after the treatment is given. At this period, there seems to be a rather marked constant factor, in that the child will stop coughing immediately after the treatment, the whooping and vomiting stopping at once.

The interesting fact that came out of these statistics was that it appeared that when the roentgen-ray treatment was given early it did not benefit at all. Seventy-five per cent of the patients who had the cough for eight or nine weeks received treatment during the first week of the disease. It is thought that this very early treatment might be harmful. The roentgen ray seems to benefit about 20 per cent of the cases; the benefit being due to some active on the pathology which is produced by whooping cough.

EMPYEMA IN INFANTS UNDER ONE MONTH. Presented by DR. W. J. CORCORAN.

Case 1.—S., a boy, was the fourth child of healthy parents. He was delivered in the home by a midwife who disregarded all ordinary rules of cleanliness.

The baby was breast fed. On the ninth day the cord came off. A cough began on the eighth day, and the mother stated that fever seemed to have been present for several days prior to this. I saw the baby for the first time on the tenth day.

The baby's body was greatly emaciated. The skin was dry and hung in loose folds. He coughed frequently and grunted with almost every breath. The navel was filthy. A large area of redness surrounded the cord remnant and the discharge had a bad odor. There was no distention of the abdomen. The spleen and liver were not palpable. The heart was normal. The breath sounds heard over the left lung were loud and rough. There were many mucous râles throughout. Breath sounds over the right lung were markedly diminished. The right side of the chest was flat on percussion, and there was a definite feeling of resistance on tapping the right side of the chest wall. The pharynx was congested. The anterior fontanel was depressed. There was no rigidity of the neck. The deep reflexes were normal, and there was no spasticity of upper or lower extremities. A large number of lymph nodules were palpable in the cervical and inguinal regions. The rectal temperature was 103 F., and the respirations were 60.

Aside from more pronounced prostration and rapid loss of weight, the following day showed few changes in physical findings. The temperature had dropped to 101 F., and the respirations increased to 70 per minute.

On the next day, the thirteenth day of illness, the baby died. Necropsy showed that the inflammation around the navel was not confined to the external surfaces. The thrombi of the umbilical arteries were infected. A probe was passed directly into the arteries from the navel. In this suppuration the umbilical vein escaped the spread of infection. Cultures taken from the umbilical arteries showed staphylococci and streptococci.

The heart, liver and spleen were normal. The right pleural cavity contained a large amount of pus similar to pea soup. The right lung was moderately compressed, and revealed a number of small areas of consolidation of the type found in babies dying from any wasting disease. The left pleura contained a small amount of reddish, serofibrinous fluid, but no pus. The left lung showed a few patches of terminal consolidation. The brain and meninges were normal. A culture of the pus from the right pleura contained streptococci and staphylococci.

This case is presented as one of empyema having its origin in an infection of the navel.

Case 2.—R., a boy, 14 months of age, was born at the Mercy Hospital. He was a full-term infant, normally delivered. He was breast fed, and made the usual progress of a healthy baby, until the fourteenth day, when he became acutely ill. Fever and cough were the only symptoms at the onset. He took the breast poorly and vomited frequently. I was asked to see the baby on the seventeenth day.

At that time he was extremely pale and emaciated. The skin was dry and harsh. The navel was clean. The breathing was rapid and grunting in character and there was a short, dry, infrequent cough. The rectal temperature was 102 F. There was some impairment of resonance over the right upper lobe posteriorly, with bronchovesicular breathing. The heart action was quite rapid. There were no other abnormal physical findings.

During the following two days the clinical findings were those of a frank lobar pneumonia of the upper right lung. Fever and prostration continued for eight days following the onset of illness. Then the temperature dropped

slowly. Coughing continued, however, and became very harsh; during these paroxysms of coughing the child cried with pain. Three days later the temperature rose to 103 F., and the coughing became more frequent. At this time there was some diminution of breath sounds at the right base, and on the following day there was a definite sense of resistance on percussion over the entire right side of the chest. The fifth day after the pneumonic condition had cleared, and the baby's twenty-seventh day of life, a paracentesis of the right pleura was done, and 60 cc. of pus was removed. The child was then taken to the hospital. Fluids were given freely, rectally and by hypodermoclysis, for two days, and then, under ether anesthesia, the right pleural cavity was opened. A large amount of pus was evacuated and the cavity drained by the open method. A culture made from the pus showed pneumococci.

A blood count made prior to the operation showed: 32,000 leukocytes; 3,800,000 erythrocytes and 70 per cent hemoglobin.

Although drainage was free the child did not rally as was expected. He became apathetic, refused his food and vomited much of that which was taken. Repeated blood analyses showed a gradual lowering of the red cells and hemoglobin. On the seventh day following the operation, the red cells were 2,200,000 and the hemoglobin 39 per cent. A blood transfusion of 100 cc. was given. For a day or two he seemed less apathetic, but there was no great change in his general condition. It was then decided to expose the child's body to direct sunlight. The lower extremities were exposed first and then other body surfaces. After several days of this treatment the baby became brighter and cried lustily at feeding time. A number of days later a second transfusion of 125 cc. of blood was given. Marked improvement occurred following this, although the first transfusion seemed to have given indifferent results.

On the twenty-seventh day following the operation the child was allowed to go home. The red cells had increased to 3,340,000 and the hemoglobin to 70 per cent. Slight drainage continued for about two weeks. During the child's stay in the hospital the mother's milk disappeared and he received whole lactic acid milk. At the time of presentation the boy was 14 months old, weighed 23 pounds, walked, spoke a few words and in every respect was normal physically.

DUODENAL REACTIONS, CHEMICAL AND PHYSIOLOGIC. Presented by DR. LLOYD ARNOLD and DR. R. A. BLACK.

The reaction of the duodenum and its effect on the individual in relation to quite a different problem than the bacterial content interests these investigators. Their experimental work was confined to quite young dogs, in which they have fastened the duodenum to the anterior part of the abdominal wall so we could enter the duodenum with a small needle and any material we wished. In that way the bacterial content and the hydrogen ion concentration could be ascertained. The usual findings of the stomach contents were supposedly acid, the limit running slightly to the acid side. From the pylorus down to the zone in which the neutral chemical reaction is obtained, the contents are practically sterile. If a needle was introduced and alkaline buffered solutions were injected, the dog had a leukocytosis of three times the normal number, and a temperature elevation of several degrees. This rises promptly and lasts for five or six hours, following which the dog recovers. Then if foreign proteins were injected subcutaneously, they caused a reaction whereby an alkaline reaction in the duodenum could be produced, a decrease in the

gastric juice was obtained, associated with which was alkalinization of the duodenum (about p_H 6.5 to 7.5). This was associated in every instance with elevation of temperature on the part of the animal, and so far as the gastric secretion is concerned, many workers have found that to be depressed.

What effect this had on the duodenal and the stomach contents was of further interest. If it is assumed that the stomach reaction is normally about p_H 0.4 and that for the duodenum as between p_H 0.4 and 0.6, with that in the jejunum about p_H 0.5 to 6.5, if a baby with some temperature elevation is seen, it is well known that the acidity comes near to the neutral reaction. The duodenal reaction does not change much. If the temperature elevation persists from three to five days, if it is excessively high or of gastro-intestinal origin, it is found that the stomach content will run about the same degree of acidity, but the duodenal content will become alkaline in reaction, and p_H 7.5 in the middle of the jejunum is obtained. Associated with alkalinization of the upper end of the small intestine is an ascension of the bacterial flora in the duodenum, but this can be broken up very easily by acidification of the duodenum.

From the pediatrician's standpoint, the use of acid milks really involves the principle of saturating all the buffers of the milk with acid and rather influencing the duodenal function instead of the stomach function. If the baby has a foreign protein intoxication and has this reaction, Dr. Black has been using a formula with one-half enough acid to coagulate the milk and feeding, so as to relieve the stomach and not allow the alkaline reaction to take place in the duodenum.

While this work was being done, a Scandinavian and a German worker have published much the same results. They explain it on a gastric function basis, but it is thought that its main function is to saturate the buffers and throw them over to the acid side so that the content of the duodenum will maintain a normal reaction. If the bile and pancreatic juice are cut out, an increase of the bacterial flora is not obtained, but as soon as the acid condition of the stomach is cut out, it is obtained.

LEUKEMIA. Presented by DR. H. W. ELGHAMMER.

A child, aged 6 years, was first seen on Sept. 5, 1925, in the pediatric clinic at Mercy Hospital, with the complaint of enlarged neck glands. She is the second of six children, all the others being well. The father and mother are well and there is no history of tuberculosis or syphilis in the family. She was a full term baby, but her mother had influenza during gestation. The first year of life was uneventful, but following that she had the ordinary diseases of childhood, and rather severe scarlet fever, followed by nephritis. During the last year, she has had a sore throat frequently and three weeks before admission her tonsils were removed.

Examination on admission revealed a fairly well developed child. The lymph glands were not much enlarged and the other findings were negative. She was put on rest, diet and ordinary tonic treatment and returned after two weeks with a gain of 2 pounds. Her general condition had improved but the glands in the neck were more enlarged. At that time we looked carefully for enlarged lymph glands elsewhere but found none. The tuberculin test was negative. She was put on sodium cacodylate and was asked to return. She came in on October 10, complaining of a slight cold. At that time the glands were much enlarged and the lymph nodes of the axillae and popliteal spaces were enlarged. The spleen was five fingers below the costal margin.

The heart, chest and other organs were normal. The laboratory findings were negative throughout, except that the urine had a slight trace of albumin. She was admitted to the hospital with the tentative diagnosis of leukemia. A section from one of the glands of the neck was reported to have lost its characteristic structure and to be composed of round cells, and was diagnosed as a lymph gland of lymphatic leukemia. The blood Wassermann reaction was negative. On the day of admission the red count was 3,800,000; leukocytes 85,000, and hemoglobin 80 per cent.

Roentgenography of the spleen, chest, long bones and cervical glands was started on October 24; there was rapid decrease in the white cells, the highest count being 200,000, until they reached 2,700. During that time there was destruction of the lymphocytes by the roentgen ray and partial destruction of the red cells, from 3,800,000 to less than 3,000,000. The hemoglobin varied. The marked adenopathy in the neck disappeared entirely. By a special count of the polymorphonuclears their regeneration can be seen, with destruction of the lymphocytes. It is thought that this child is in rather a critical state.

FRIEDREICH'S ATAXIA IN TWINS. Presented by DR. JULIUS H. HESS.

Twin boys, aged 15 years, two of seven children in the family, were presented. They were well until 1917, when the entire family developed influenza. Before this illness, these boys had been in the habit of giving physical exhibitions at various entertainments and were in splendid condition. Their convalescence from the influenza was slow, and it was noted after a few weeks from the onset that they were irresponsible and did rather foolish things. They first came to the County Hospital in 1920, and at that time they were both having difficulty in coordinating their movements. They had not been in school since their attack of influenza because of inability to coordinate their mental activities, but before that they had made good progress. They both had a masklike expression, both had slight nystagmus, and when first seen both had difficulty in controlling their movements. Both had disappearance of the reflexes in the lower extremities but they were present in the upper. Both had scanning speech, pes cavus, and both were developing scoliosis. They returned to the hospital after four months and at that time one boy could take pretty good care of himself, could button and unbutton his clothes, but the other boy had lost the ability to undertake finer movements.

They entered Michael Reese Hospital for observation in 1924, and by that time one boy had lost the deep reflexes in his upper extremities. Both of them have marked nystagmus, the movement being toward the side to which they are looking. I believe there is cerebral, cerebellar and cord involvement in both cases. In most of the reported cases of Friedreich's ataxia there has been involvement of the crossed pyramidal tracts, the columns of Goll and Burdach, Gowers' tract, the direct cerebellar tract, and less often of Lissauer's tract and the column of Clark. The disease is undoubtedly progressive. At times these boys are mentally much better than at others. Sometimes they become irritable but most of the time they are quite good.

The question in our minds is whether these cases may not belong to the atypical encephalitis group which we have been seeing since the first epidemic of influenza. I believe, however, the findings are typical of Friedreich's ataxia, and even in the absence of any family history they have been so classified. Many of the reported cases of Friedreich's ataxia became manifest after an acute infectious disease.

FURTHER REPORT ON ROENTGEN-RAY TREATMENT OF PERTUSSIS. Presented by DR. JULIUS H. HESS.

I was absent when Dr. Black gave his findings in pertussis, but hope we agree on the conclusions. We divided our 102 cases into two groups, the summer and fall, and winter and spring. We had sixty-two cases in the first group and were quite certain that the treatment caused considerable improvement in 43 per cent. I think we will always have some cases with striking results. Then we had forty cases in the winter and spring months and found 25 per cent showed improvement, but in 47.5 per cent we decided there was no improvement. I think there is no such thing as prophylactic use of the roentgen ray. Even when it was used before the cough was well under way, many patients showed no improvement. We found that the patients in whom it did the most good were those in whom it was used during the second or third week. In 50 per cent of the cases in which we thought we saw results, the improvement was obtained from one treatment. In only a few did we give three or four treatments. We never saw any results from vaccine following roentgen ray therapy. We had some patients in whom the vaccine had been given previously in from one to four doses, without evident improvement, in which the roentgen-ray therapy seemed to be associated with some change. We felt that in the cases with a high leukocyte count, with the lymphocytes predominating we obtained the best results, and as a rule in those cases there was a considerable change in the blood picture. We had six cases complicated by pneumonia, and I think if I saw striking benefit in any patients those were the ones.

I would certainly say that roentgen-ray therapy is not a "cure-all" for whooping cough. The most that should be expected is relief of the vomiting and reduction in the number and severity of the coughing spells, while in some cases the course is shortened. I would never tell a parent that a child could be cured, for I think it dangerous to carry the treatment to three, four or more exposures. The thymus is always exposed to the rays and it is close to the thyroid. I believe the method is indicated in selected cases as symptomatic treatment.

PHOSPHORUS METABOLISM OF NORMAL INFANTS. Presented by DR. DAVID B. WITT.

This work is part of the study of the various mineral constituents in a comparative study of the metabolism of cow's milk and breast milk in the same infants. During the period in which these infants were fed diluted mixtures of cow's milk, not only was the intake of phosphorus greater but there was also a larger quantity of phosphorus excreted in the urine and the feces. Despite this, the percentage retention of phosphorus was greater during the periods when the infants received breast milk.

PYLORIC STENOSIS IN A CHINESE BOY. Presented by DR. MARK JAMPOLIS.

A boy, aged 6, was born in China, and was admitted to Michael Reese Hospital on July 23, 1925. He was breast fed and never vomited in infancy. Vomiting never occurred, except with occasional attacks of fever, until three weeks before his admission to the hospital. On July 3, he began to vomit one or two hours after taking food. Sometimes he complained of pain half an hour before he vomited. It was stated that at that time the vomiting was not projectile. This continued for about a week when it suddenly stopped

and he was well for over a week, but on July 19 he again began to vomit. At that time it was increased in severity and he vomited everything that was ingested immediately after it was taken into the stomach. When he was admitted to the hospital he was markedly emaciated, had lost several pounds in weight and there was extreme dehydration. The temperature was normal, there was no blood in the stools or vomitus, but the patient showed some leukocytosis. He showed the largest gastric peristaltic waves that we have ever seen here. They were two or three times as large as the waves in infants. A roentgen-ray picture was taken after two hours and showed complete obstruction of the pylorus, which was unmistakably palpable. At the beginning of the attack he was treated with Chinese drugs and for two days before admission had been given atropin by mouth, without result. Dr. Harry Jackson operated on the boy, and found a large tumor of the pylorus and stenosis. It was 3 inches long, over half an inch thick, and was very tough and fibrous. He attempted pyloroplasty but was unable to relieve the obstruction because it was so large, so he performed a gastro-enterostomy. The boy made an uneventful recovery and the stomach now empties normally, as proved by roentgen-ray examination. I have not found in the literature a report of what seems to be a congenital hypertrophic stenosis appearing at this late age.

Cystic Hygroma. Presented by Dr. Ethel M. Davis.

This child has been under observation in the outpatient department for several weeks, and is at present 6 weeks old. He had been entirely breast fed up to the time of admission to the hospital. The mother thinks the condition has been present since birth, and the masses are increasing in size. The swellings are located on the neck, in the right axilla and in the pectoral region. They are soft, semifluctuating masses, which can be transilluminated. Firmer masses are imbedded in the center of the tumors, over which the skin is adherent in several areas. Several days ago, about 7 cc. of a clear, lymphoid fluid was withdrawn, which coagulated on standing. Chemical analysis revealed 47.0 mg. of sugar, 14.0 mg. of nonprotein nitrogen and 0.9 mg. of creatinin per hundred cubic centimeters.

In the question of treatment, the mortality of the patients treated surgically has been quite high, 43 per cent for those in the neck and a little less for those in the pectoral region. The condition is apt to undergo carcinomatous changes. The opinion expressed in the literature seems to be that unless there are pressure symptoms, or marked, rapid increase in size it is best not to interfere unless the growth can be completely removed at one time. This subject will be given the benefit of radium treatment before surgical removal is attempted.

Subacute Meningococcus Meningitis. Presented by Dr. P. Rosenblum.

The condition of this child is of interest in emphasiing a procedure which, I think, has been neglected, and is not used as often or as early as it should be. The child, aged 3½ years, became sick about July, 1, with the usual symptoms of meningitis. She came under our care about ten days later. A diagnosis of meningitis was made, and antimeningococcus serum was given intraspinally and intravenously, rather intensively, daily and every other day for four weeks. The temperature and meningeal symptoms persisted, and after four weeks she began to have rather severe reactions from the serum, so severe that we hesitated to give any more. Also, the spinal fluid did not show any more organisms and we waited before giving more serum because

of this. The child became worse, and after two weeks had more vomiting, more headache and more rigidity of the neck, so we gave 30 cc. of serum intraspinally for four days. The temperature went up to 105 F.; as the child became progressively worse I decided to do a cisterna puncture. Forty cubic centimeters of fluid was removed by this method and 30 cc. of serum was injected. The fluid obtained from the cisterna puncture was altogether different from that obtained by spinal puncture. It was distinctly xanthochromic. Following the cisterna puncture the temperature rose to 107 F. and the child was very ill. However, the temperature came down gradually, another cisterna puncture was made and another 40 cc. of fluid removed. On that occasion the temperature rose to 105 F. but dropped more rapidly, reaching normal in twenty-four hours, following which the child made an uneventful recovery.

This method was started in 1912 by Haynes and Kopetzky, and was then dropped because there were two or three bad reactions. It was taken up again in 1917 by Anton and Schmieden, but only since 1920 has much work been done. There have been 300 cases reported from the Massachusetts General Hospital, with no untoward results. I believe we would have better results if the treatment were used earlier in the subjects who do not recover with treatment by the usual lumbar route.

CIRCUMSCRIBED, PERFORATING TUBERCULOSIS OF SKULL. Presented by DR. D. C. STRAUS.

This child was born following a normal, spontaneous delivery, weighed 7 pounds at birth, was normal in every way, was breast fed and perfectly well until January 1925. At that time he pinched one of his fingers with a toy. The finger became red, and was painful; a physician made an incision and said some pus came out. The child also had a swelling in the left temporal region, another in the frontal region, one over the ninth right rib, each of which developed following a local trauma, and a skin lesion on one leg. Physical examination showed nothing else abnormal, except some enlarged cervical glands. The chest was negative except for the rib. There was no enlargement of the liver or spleen; the reflexes were normal. The leukocyte count was 32,800, the bleeding and clotting time were normal. The roentgen-ray examination, made soon after entrance to the hospital, showed this definite clear-cut defect in the frontal region, and the lateral view, in addition to that, showed a suggestion of a defect in the left temporal region. The roentgen ray of the chest showed definite erosion and swelling of the ninth rib on the right. A diagnosis of tuberculosis was made.

The Pirquet test was strongly positive and following this the temperature rose. I advised operation, with radical removal of both skull lesions, to prevent the development of tuberculous meningitis, and resection of the rib to guard against the development of tuberculous empyema. The first operation was performed on April 20, at which time the frontal skull lesion was removed. The temporal skull lesion and the tuberculous rib were removed about two weeks later. Following the first operation there was a marked rise in temperature, and I think that this reaction was comparable to giving the child a subcutaneous dose of tuberculin. There was no special rise in temperature following the second operation, which was probably due to the fact that following this operation there was practically no tuberculous tissue left. In these patients, it is essential to go well beyond the tuberculous focus and remove it as one would a malignant neoplasm. This child made an uneventful recovery and so far is perfectly well.

JUVENILE TABES. Presented by DR. H. W. CHENEY.

This girl has been under observation for several years, and it is believed that she represents a mild, or arrested case of tabes. She was first seen about eight years ago, when she was 8 years old. The pupils did not react to light or in accommodation, the knee-jerks were absent and there was a definite family history of syphilis. She was placed on iodids but the condition continued the same, until 1920, when she had a course of neo-arsphenamine, which was followed by iodids later. Her vision was 6/10 in one eye and 6/12 in the other. The Wassermann reaction was still positive. She had another series of treatments with neo-arsphenamine and some mercury after that. The Wassermann reaction remained positive and during the past summer she had a third course of treatment, but the Wassermann reaction remained unchanged. She seems to be normal except for the following symptoms of tabes: There is slight swaying with closed eyes, the pupils are still fixed and the knee-jerks remain absent. She was a little backward in school and has now gone to work. She has been transferred to the adult department and the antisyphilitic treatment will be continued.

ALBUMINURIA. Presented by DR. J. K. CALVIN.

In an attempt to determine the possible causes of non-nephritic albuminurias, which at present are classified in a confused group of benign, physiologic or growth albuminurias, we analyzed two groups of children in largely different environmental and physical conditions. The first group consisted of children having no special complaints or illness. They were recruited from the homes of the very poor, in which hygienic conditions were at their worst, diets were improperly balanced, teeth and tonsils neglected, with undernourishment and anemia common. About 200 of these children were examined, the sexes being about equally divided and the average age 8 years. Approximately 40 per cent were underweight; 70 per cent had carious teeth or abscesses, 75 per cent had not had the tonsils removed, and most of them had had one or more of the acute contagious diseases. Albuminuria varied from a trace to ++, 40 per cent of the boys showing albumin and 60 per cent of the girls. About 12 per cent showed microscopic findings varying from pus cells to casts. The second group consisted of children living in a well regulated orphan home, under the supervision of a watchful physician. Their hygienic surroundings were good, foci of infection were eliminated as soon as discovered and periodic physical examinations were made. About 350 of these children were examined, the sexes being about equally divided and the average age 11 years. In this group 10 per cent of the boys and 20 per cent of the girls showed albuminuria. Of the boys, 15 per cent of the 90 per cent that were negative on the first examination were positive six months later, and this was likewise true of the 80 per cent of the girls who were negative on the first examination. Of the boys, 20 per cent of those positive had microscopic findings, and of the girls 50 per cent of those positive showed pus or casts. Morning and evening specimens from these subjects showed that most of them were not orthostatic (acetic test). These figures seem to indicate that elimination of toxic products from foci of infecion, poor nutrition, anemia, poor physical condition, etc., interfere with the proper functioning of the kidney, causing transitory albuminuria, but that albuminuria in a lesser incidence also occurs in children living under normal hygienic conditions. In our albuminuria clinic we have classified these cases as transitory, orthostatic and nephritic. We consider the transitory cases as

a functional condition and many of these cases respond to eradication of foci of infection, improvement of nutrition and weight and to overcoming an anemic condition. About 25 per cent of them continue intermittently despite treatment, reaching their maximum incidence during the period of rapid growth during puberty. The urea determinations by the Hench and Aldrich method of salivary urea estimations have been made on many of these subjects, and normal values were found.

IDIOPATHIC CARDIAC HYPERTROPHY IN AN INFANT. Presented by DR. I. A. ABT.

This infant, female, was 8 months old at the time of death. She was born under normal conditions, of healthy, young parents. The mother shows neuropathic tendencies but is otherwise normal. The baby was artificially fed and gained moderately in weight, but when she was 3 months old it was found that she was extremely difficult to feed, and most of the feedings were forced. She frequently became cyanotic during these struggles, but in the intervals she was happy, slept normally and was slightly pale. The child was repeatedly examined, and a short systolic murmur was heard in the third intercostal space to the left of the sternum. The apex beat was several centimeters to the left of the mammary line, and the right border seemed to extend considerably beyond the midsternal line. The child was taken suddenly ill on the morning of September 17, with dyspnea, cough, cyanosis, and crying attacks, as if in great pain. The temperature was moderately elevated, the pulse was small and rapid. Examination showed a definite and considerable increase in the cardiac area, a distinct systolic murmur, and numerous small, fine râles in the posterior portion of the left thorax, with an extensive area of dulness in this region. The dyspnea, cyanosis and crying continued, and on the evening of this day the child suddenly expired.

Necropsy was performed the same evening. The heart, measuring 8.5 by 5.5 by 5.5, was characterized by extreme hypertrophy and dilatation of the heart muscle, particularly of the left ventricle. The coronary arteries were markedly curled, prominent and felt firm. Both ventricles were distended and the left felt soft. On the cut surface the heart muscle appeared yellow, and in other areas was light red. The papillary muscles were flat and soft, and the cords and flaps of tricuspid valve were thin and delicate. The right auricle was nearly empty and the foramen ovale closed. The anterior wall of the left ventricle showed marked bulging and the apex was increased in area. The mitral valves were delicate, thin and movable. The cords were thin and elongated. The aortic valves were competent; the semilunar cusps were thin, translucent and complete. On section, the lungs were dark bluish-gray, and on pressure a frothy liquid escaped. The kidneys showed a few hemorrhages the size of a pinpoint, though the cortex showed normal structure and markings and there were no abnormalities in the medulla. In the microscopic examination, the lower portion of the left lung showed some atelectasis. The muscle fibers of the heart seemed to be pulled apart. The normal markings of the fibers were indistinct. The nuclei stained poorly. All blood vessels and capillaries were engorged with blood. In some areas the muscle fibers were vacuolated, and some areas showed, in addition, necrosis. The endocardium in some places was edematous and separated from the muscle. There were numerous areas of round-cell infiltration and phagocytes containing hemosiderin. The thymus was not enlarged and did not seem to encroach abnormally on other organs, causing pressure.

Anatomic diagnosis was extreme hypertrophy and dilatation of the heart muscle, especially of the left ventricle; chronic and recent infarction of the musculature; necrosis and hemorrhages; thickening of the endocardium; fatty degeneration of the left leg of the bundle of His; generalized congestion of the heart muscle; hemosiderosis of the lungs, spleen and kidney; extensive atelectatic areas in both lungs.

SURGERY OF HYDROCEPHALUS. Presented by DR. G. L. DAVENPORT.

It is believed that four-fifths of the cerebrospinal fluid is absorbed in the region over the cerebral hemispheres and one-fifth over the spinal cord. I think it is accepted at present that there is either an over-production of fluid, lack of absorption, or both conditions, due either to congenital or acquired causes. In the operative procedure for intra-abdominal drainage, we drill a hole through the body of the fifth lumbar vertebra and insert a glass tube. Other methods we have used in these cases consist of multiple or frequent ventricular, cisternal or spinal puncture, repeated at such times as we find necessary in our effort to re-establish the fluid balance. We believe if the patients are seen early, the possibility of a cure is better than when they are seen later. In the later stages there is a blocking off and pocketing of the fluid in various places, especially at the base, which prevents the proper circulation of the blood and also the circulation and absorption of the fluid. We have found the specific gravity of the fluid in these infants averages 1,008 to 1,010. In some subjects, after the introduction of air into the ventricles with the insertion of a needle into the spine, as in lumbar puncture, with the baby held up by the feet (head down) there would be an out-rush of air through the needle. This led us to practice the following procedure: After the introduction of air into the ventricles, the patient is turned gently first head up and then feet up, several times each day, hoping that in this way the air, being forced from one extreme portion of the system to the other, will break up the adhesions and stimulate absorption of the fluid.

Case 1.—This patient originally had spina bifida of the meningomyelocele type. We thought it best to close this off early, to avoid infection if possible. We succeeded in getting the desired result in the spine, and also the concomitant hydrocephalus which we expected. We then resorted to intra-abdominal drainage by way of the fifth lumbar vertebra, but this was unsuccessful, as we expected, because the fluid did not reach below the level of the operation for spina bifida.

Cases 2 and 3.—In these two cases of hydrocephalus we withdrew almost 150 cc. in the first case about five days before presentation, which at the time of writing had not yet refilled. In the second case we withdrew several cubic centimeters and it refilled within a few hours.

Our results in a small series of cases have not been very encouraging, but there has been an occasional cure and an occasional arrest of the process.

FURTHER OBSERVATIONS ON THE TREATMENT OF CHOREA BY ROSENOW'S SERUM. Presented by DR. J. R. GERSTLEY and DR. KATHERINE HOWELL.

Our conclusions in this work will be given briefly. As you know, Dr. Rosenow claimed to have discovered the specific cause of chorea, in a non-hemolytic streptococcus. He was kind enough to send us some of the serum, which we have used for two years in our wards. We treated every second cast with the serum, in doses of 10 cc. over a period of seven to ten days, but

were not able to see any influence of this serum either on the immediate disease, on the course and duration of the disease, on the course of complications, or on the development of recurrences. This was rather disappointing. The immediate results were bad because of the development of serum sickness.

We also endeavored to find if there was any particular strain of streptococcus, and whether the serum agglutinated any particular streptococcus. We made about 120 nasopharyngeal and tonsillar cultures of which twenty to thirty showed a hemolytic streptococcus, sixty showed a nonhemolytic, and the remainder showed no streptococcus. We found that the serum agglutinated both the hemolytic and nonhemolytic, so we are forced to conclude that the serum is not specific in its present form. We have been unable to produce the syndrome in rabbits which Rosenow described, and we consider that the serum in its present form is of little value in the treatment of chorea in children.

METABOLISM OF UNDERNOURISHED CHILDREN. Presented by DR. CHI CHE WANG.

During the last four years we have made a careful study of undernourished children, and have observed forty-four subjects in all. Some of the children remained with us for two weeks; others stayed until they had reached normal weight. One child was with us for five months. We studied nitrogen and mineral balance and basal metabolism. The present report deals with the gain in weight of the children, and a somewhat more detailed study of the child who remained for five months. The children were sent to us from nutrition classes in which they had failed to gain weight, but during their residence at the hospital all the children increased in weight and this increase was far in excess of that to be expected in normal children. Every child who was with us longer than two weeks gained more while here than a normal child of the same age gains in a year. (The chart showing the curves will be published later.)

Annie, a Jewish girl, aged 10 years, was 27 per cent underweight when she came to us. She had been in the hospital for two weeks two years previous to her long stay, and was then 26 per cent below normal weight for her age and height. During the two years she had made no progress whatever, but after five months with us she was only 7 per cent below normal. Her basal metabolism during her first stay was 17 per cent below normal for her height. The second time it was 7 per cent below normal when she came, but as she gained in weight her metabolism increased, and when she left was 1 per cent above normal.

The excretion of creatin and ammonia nitrogen in the urine varied with the diet, increasing as the protein intake increased. Creatinin increased as body weight increased, but the amount per kilogram of body weight remained almost constant.

QUANTITATIVE FEEDING. Presented by DR. A. LEVINSON, MISS R. S. ECKMAN and MISS BLANCHE TUDOR.

A study of food service was made in the Sarah Morris Memorial Hospital, as a preparatory measure toward formulating a schedule of food portions that would enable a physician to designate to the nurses the quantities and types of food and the caloric values he wishes to have consumed by the children. The proceeding gave us a great deal of information concerning the average consumption of each type of food, the popularity of certain articles of food and the amount of food wasted during the meal service. The group studied

consisted of twenty children between the ages of 5 and 12 years. The study lasted six days. The children were not forced to eat but were supervised and encouraged during their meals. The food was weighed out in bulk before it left the kitchen and the returned food was weighed, as well as all plate waste. The number of trays served at each meal was noted. From these data was determined the total consumption of food, the average consumption per child and the average calories of energy ingested.

From the tabulated results we found the percentages of waste as follows: Cream soup, 61 per cent; all vegetables, 49 per cent; all cereals, 46 per cent; protein dishes, 42 per cent; toast, 29 per cent; fruit, 12 per cent; cocoa, 19 per cent; milk, 15 per cent; butter, 20 per cent. We found in this short study the value of supervision. Unless children are supervised at mealtime, many of them will not take enough of the proper kind of food. Quantitative feeding is of special importance when it is desired to give children concentrated feeding as advocated by Schick, Nobel and others. It has also been found useful in children who refused food in cases of edema or of exudate into some body cavity, and in some cases of enuresis.

TYPES OF LOCALIZED MENINGITIS. Presented by DR. A. LEVINSON.

The diagnosis of localized meningitis is of more than theoretic importance. During the past four years we have seen three cases in which the diagnosis was quite well established. One patient came into the Sarah Morris Memorial Hospital with fever, and the cerebrospinal fluid showed meningococci. The symptoms were unilateral and the original diagnosis was brain abscess, despite the finding of the meningococci in the fluid. At operation no abscess was found, and on necropsy the meningococci were isolated both in smear and in culture.

In the second case the patient presented some symptoms suggestive of poliomyelitis, but the cerebrospinal fluid showed meningococci and after the intraspinal administration of antimeningococcic serum the child recovered.

The third case was clearly a brain abscess with superimposed meningeal symptoms. The first symptoms were headache and choked disk, vomiting, and the other signs of meningitis developing later. The child was operated on and made a good recovery. The cerebrospinal fluid contained many cells, a good deal of globulin and the Lange test gave a meningitic curve for a few days.

In every case that presents acute symptoms with unilateral nervous findings, one should bear in mind the possibility of meningitis. When the diagnosis of meningitis is made, an attempt should be made to separate the primary from the secondary forms. If the infection is primary, serum should be given. If it is secondary, especially to brain abscess, operation should be resorted to, as this offers the best chance of recovery.

GAUCHER'S DISEASE AND LIPOID HISTIOCYTOSIS. Presented by DR. WILLIAM BLOOM.

In the Michael Reese Hospital we have had two cases of Gaucher's disease and three cases of what I shall call Niemann's disease. In the latter the children do not thrive on any type of food. There are four cases of this disease in the literature, which have been considered by some as examples of Gaucher's disease.

Histologically, the changes are striking. Gaucher's disease involves only the spleen, lymph nodes, bone marrow and liver, whereas Niemann's disease

affects besides these organs the lungs, suprarenals, thymus, kidneys, and loose connective tissue throughout the body.

The main difference between Gaucher's disease and Niemann's disease is that the material filling up the phagocytic cells in Gaucher's disease is a protein — probably a cerebrosid — whereas in Niemann's disease it is a complex lipoid. The cell involved in both conditions is undoubtedly a part of the reticulo-endothelial system.

Of our three cases of Niemann's disease, one was a postmortem finding; one was diagnosed during life by splenic puncture. The blood lipoids were normal in amount. The child died several months after splenectomy. The third case was diagnosed at necropsy because of the highly suggestive salmon color of the spleen. This child died of meningitis.

To avoid the eponym, we would suggest for this condition the name "lipoid-histiocytosis."

SURGERY OF INTESTINAL ANOMALIES. Presented by DR. A. A. STRAUSS.

We have divided these intestinal anomalies into three classes. First, those patients who should be operated on immediately after birth; second, those within a week or so after birth and, third, those that do not manifest the condition until several years after birth. There are a number of intestinal anomalies for which operation should be performed within the first few hours after the child is born. To the new-born infant we can give ether with little shock, and within a few hours after operation can give the child to the mother to nurse and she will never know it has been operated on until she is home from the hospital.

One of the anomalies which is usually allowed to go on is the hernia through the abdominal wall. The intestine in the hernia makes traction on the mesentery, and there is hemorrhage into the bowel; if operated on twenty-four hours after birth the child will die, no matter how efficient the surgeon, because the intestines have been damaged. If operated on within an hour after birth there will be an uneventful recovery.

The next condition to which I wish to call your attention is esophageal stenosis, of which we have had four cases. These patients may have partial obstruction and not come to the attention of the surgeon until one or two years have passed. There will be a history of taking liquids but not solid food. Many of these are treated by esophageal dilatation, many of them are ruptured and the child dies of pneumonia. We have operated for this condition directly through the abdomen. The pathology in all four of our cases was exactly alike. We cut away the adhesions and pulled the esophagus through. We passed a catheter through, then passed an instrument up and dilated it and made a longitudinal incision through the muscularis down to the mucosa. This will dilate the esophagus and within four days the child can eat solid food.

It is interesting that in addition to the congenital esophageal stenosis, one child had pyloric stenosis, Meckel's diverticulum and a nonrotated cecum.

Another type of anomaly is the atresia of the duodenum beyond the ampulla of Vater. One patient came in with the diagnosis of pyloric stenosis, did not have a roentgenogram made, and was treated with atropin and diet. The child was brought back nine months later. The roentgen ray showed a dilated duodenum, the pylorus was dilated almost to the width of the stomach, and there was an adhesion below the ampulla of Vater that closed the duodenum. A gastro-enterostomy and pyloric closure was performed, and the child made

an uneventful recovery. If the pylorus is closed down, the duodenum will contract because no food goes through it. We have had one other case of duodenal atresia that was so slight that the child recovered without operation.

The types of anomalies that show up two or three years after birth are interesting. Among them is Meckel's diverticulum, which has produced hemorrhage. This gives the symptoms of bleeding duodenal ulcer, with tarry stools and the resulting anemia. We have had four of these cases. The first was not recognized as Meckel's diverticulum. We made a V-shaped incision, incising Meckel's diverticulum, an end-to-end anastomosis and the child made an uneventful recovery. We gave two blood transfusion before the operation. In another case of bleeding Meckel's diverticulum, the first symptoms occurred at the age of 2 years. All the children between birth and 18 months showed the symptoms of duodenal ulcer. In every child about 2 years of age who has tarry stools, and in whom the roentgen ray shows nothing in the duodenum, we must think of bleeding Meckel's diverticulum. Another type of case is the infant with an imperforated anus. Many times a child is born in the maternity hospital and the obstetrician leaves it alone for twenty-four hours. These infants should be operated on immediately for two reasons: the operation is simple and will release the meconium. If the patients are not operated on, they may become toxic and die. If it is not a simple case and the child is operated on within an hour, we sometimes find that there is a connective tissue remnant that extends through the greater part of the perineum. In these cases we advise an immediate colostomy and further surgical interference later.

We are convinced that new-born children can be operated on within an hour after birth under ether anesthesia, without loss of blood and without shock. They usually make an uneventful recovery.

A Case of Death Anxiety in a Child. Presented by Dr. David M. Levy.

This girl, aged 11 years, was brought to the Sarah Morris Memorial Hospital in September, 1925, because of acute attacks in which she would pant, scream "my heart is stopping," speak with a peculiar stammer, and run her arms over her chest and abdomen with constant arrhythmic movements of the head and trunk. Associated with these facial movements were grimacing and ticlike movements of the lips and tongue. In the hospital she would usually lie flat on her back with her legs spread wide apart. These attacks had begun six months previously, when her mother first noticed that she would become suddenly excitable, tremble all over, say "I don't feel good, I got a flutter," put her hand over her heart and shout, "I'm dying!" They occurred once or twice daily, with increasing severity, and by August they had assumed the severe form just described. Since the onset she had refused to play with other children or go to school, because of fear of dying. Physical examination was negative. She has now been free of the acute symptoms for five weeks, has been attending school every day, and has resumed her play with other children.

The child is presented not as an example of therapeutic success, since the time has been too short to make certain of her recovery, but to show the striking relationship between such acute anxiety crises and the inner mental conflicts, with their immediate response to psychotherapeutic measures. These measures are an adaptation of psychanalysis to the problems of childhood, a procedure necessarily more active than in adults and in the form of direct interview, with free association to words propounded by the analyst. With children it is important to shorten the analysis considerably as compared with

the adult, since the analyst quickly becomes the "new father" and the re-adaptation to the real parents difficult. It is often advisable to utilize the services of a psychiatric social worker in the end stage, without personal contact with the patient.

The death anxieties in this child were related to death wishes for the sister whose arrival six months ago removed her prestige as an only child; then to the mother, whose death would satisfy her longings for the father; finally, to her fear of pregnancy, which was in reality the major symptom and which expressed itself in some of the movements observed, and in her wish to have the child herself. These conclusions are the result of direct responses to the active interview, and to the observed behavior, that is, actual threats on the child, calling her father to her bed and insisting that he sleep with her during such anxiety attacks, and so forth, all checked up by the parents.

The sequence of events on which the acute attacks were developed are as follows: Between the ages of 4 and 9 years, she had numerous sex experiences with a girl cousin, who inserted sticks, and other things, into her vagina in the game "hospital," and kissed her nipples, thus stimulating especially the vaginal and nipple areas. (The nipples were rubbed as part of the "anxiety" movements and were masturbatory.) At about 4½ years she accidentally discovered her adult uncle with an erect organ in the toilet. This memory was later used in the sex phantasy in which this organ, like the sticks, was inserted into her; then finally the father, although she knew nothing about coitus. From her fifth to tenth year there was much stage dancing, which won her much applause and helped to accentuate the spoiling she already had from young, overly fond and proud parents, and thereby aggravated the usual reaction to the on-coming child. Her stage work gave her much poise and self-assurance, which helped to make her the leader of her school group, as she always was. At ten years came the mother's pregnancy, and her erroneous and incomplete accounts of sex, which did not allay but stirred the child's already stimulated curiosity. This showed itself in her constant manipulation and examination of her own genitalia, looking for the "seed;" examining her feces, expecting to see parts of her body or the child within her; much somatic sensation of her own pregnancy, which she thought might have been started by a boy who mischievously called her fat and forced a ruler to her anus. When she was about 11 she observed her baby sister in a convulsion, which she took on in her "death crises," the breathing difficulty in her stammering, and the mouth movements of her early body kissing experiences with her cousin. The rest of the attack is explainable on the basis of the coital act, the birth act and the nipple movements. In this manner the single elements of the anxiety crises can be traced to their origin. The therapy is not explainable on the exercise of the analytical method, although the alleviation of the difficulty through its understanding is a significant factor in treatment. It is through the release of the emotional force directed away from the conflicts enumerated into the phenomenon of the "transfer" that is the basic step in cure.

REGISTRATION OF PERISTALSIS BY THE EINTHOVEN GALVANOMETER. Presented by DR. I. HARRISON TUMPEER and DR. PAULINE W. BLITZSTEN.

As the electrocardiograph is a means of registration of the current produced by the contraction of the heart muscle, it would seem possible to obtain a graph from the contractions of the gastro-intestinal tract. The visible peristalsis in infants with pyloric stenosis is particularly suitable for this purpose. With the assistance of our former electrocardiograph technician, three years ago I

attempted to obtain tracings without success. We placed the electrodes over the cardiac and pyloric regions. Experts discouraged the application of the Einthoven galvanometer for this purpose. In the meantime Alvarez of California published his results in an old woman with pyloric obstruction and visible peristalsis. He termed his tracing the first human electrogastrogram.

This year, Dr. Blitzsten, the director of our electrocardiograph department, and I resumed this study with interesting results. We decided to take the regular three leads and note the effects on the electrocardiograph tracing of such counter or interfering currents to be expected in the exaggerated peristalsis of pyloric stenosis. The visibility of the peristaltic movements offered a control on the one hand, and the normal electrocardiograph curve offered a norm for basis of comparison on the other. We obtained tracings. At first, the usual heart tracing on a regular base line can be seen. Then as the peristaltic waves begin to cross the abdomen, the base line moves upward and downward and later returns to the normal base line. This may be compared with the tracings we obtained ten years ago by the balloon method. The tracings are much alike, and confirm Alvarez's contention that the electrogastrogram resembles the mechanical tracing. During the course of this work we checked by a second method, namely, a tambour tracing with the tambour over the epigastrium. I wish also to report that similar results were obtained in a child with Hirschsprung's disease, whose vigorous intestinal peristalsis could be seen coursing over the abdomen. Similar to the latter was an accidental graph obtained while an infant had a bowel movement. A rise was seen in the tracing when no peristalsis was visible and the infant appeared asleep.

Development of Craniotabes in Vomiting Infants. Presented by Dr. I. Harrison Tumpeer.

There is a large group of infants that are called "pylorospasms" because they vomit. These infants are distinguished from those with hypertrophic pyloric stenosis chiefly because of the absence of a pyloric tumor on palpation or on operation. Roentgen-ray examination does not necessarily demonstrate delayed emptying time. Delayed emptying should be constant in a pyloric spasm. The therapeutic test of atropin administration is fallacious. Atropin has no selective action on the pylorus. Atropin abolishes all peristalsis. Seven years ago we found in animals absolute and regular cessation of gastric peristalsis within six minutes after the subcutaneous administration of atropin. The diagnosis of pylorospasm cannot be based, therefore, on the so-called therapeutic test, and the roentgen-ray findings are inconclusive. To what class do these vomiting infants belong?

In fourteen such infants whom I have followed, I have noted the appearance of craniotabes at 4 months of age, whether or not breast feeding was supplied, and despite the routine administration of cod liver oil and orange juice at 3 months. What was the significance of the development of craniotabes in this type of infant? Speculation immediately suggested the spasmophilic diathesis. With the limited means for investigating in private homes, further observations were made to connect the infant's vomiting and craniotabes with a spasmophilic inheritance. These infants are hyperactive, incessantly moving about and awakening at a slight noise. As they grow older this behavior is more marked, and then the Chvostek sign appears. The Chvostek sign will be found in the mother usually and sometimes in the father of the infant. It requires little study to determine from which parent the hyperirritability is derived. Still

more interesting is the fact that if you go further into the family history the grandmother will tell you that all her children were vomiting infants, and that the mother of the child vomited everything in early infancy although she gained in weight. The older clinicians described nervous vomiting and stated it occurred in nervous families. There is nothing new in the description of nervous vomiting. The finding of craniotabes which suggests spasmophilia, the further development of hyperkinetic behavior and the Chvostek sign in these very children, the finding of the Chvostek sign in the parent and the occurrence there of hyperirritability, the further history of vomiting in the parents are more concrete data which indicate that so-called pylorospasm is an early manifestation of the spasmophilic diathesis. Further evidence supporting this hypothesis is accumulating.

Book Reviews

THE YOUNG DELINQUENT. By CYRIL BURT, M.A., D.Sc., Professor of Education in the University of London; Psychologist in the Education Department of the London County Council. New York: D. Appleton & Company, 1925.

According to the author "The purpose of the book is primarily a practical one; to enable the busy reader to gain some notion how the criminal in the making may best be studied and handled." The book contains over 600 pages of fine print, apportioned into thirteen chapters, with from six to twelve subdivisions abundantly supplied with footnotes, plates, and bibliographic data. The presentation of the material, both as to scope, arrangement and thoroughness, fulfils the requirements of a treatise on deliquency which should be read by every student of this great social problem. The discussion of the subject is taken up on the following plan:

Problems and Methods; Hereditary Conditions; Environmental Conditions within the Home and Outside the Home; Physical Conditions (Developmental and Pathologic); Intellectual Conditions (Subnormal Intelligence, Supernormal and Special Abilities); Temperamental Conditions (Instincts and Emotions, comprising two chapters); General Emotional Instability (Habit Formation); Sentiment and Complexes; Neuroses. Each of these fields of approach is adequately covered by summary of the literature, descriptive case material, and the author's own conclusions. Burt's evaluations are sane and wholesome, doing justice to the facts at one's disposal without yielding to the common temptation of optimistic prophecy. For example, in dealing with the topic of heredity he says, "A mere surmise, a mere impression, or a mere *a priori* argument cannot be accepted as cogent or conclusive. Hereditary and congenital traits are not to be deduced solely from the nature of the criminal actions themselves, however abnormal or persistent. They can only be inferred, and then not always with certainty." And again, speaking of glandular treatment, "At present, such treatment is little more than experimental. With the majority of subjects treatment along social and psychologic lines must remain more urgent and effective than treatment by medical or by surgical means."

The author's analysis of social and psychologic procedures and therapeutic results is equally fair and reasonable, and gives one an idea of the legal and sociologic facilities of Great Britain, which should be enlightening to many workers in our own country who seem to believe we are unique in progressive thinking along these lines. With all that Burt has to offer, it seems a pity that "The Young Delinquent" could not have been condensed to be of real use to the busy practitioner who needs its message, yet who has not the time to put into a detailed study of this volume, which alone would enable him to get its contents.

BONE SARCOMA. By E. A. CODMAN, M.D., Registrar for the Registry of Bone Sarcoma of the American College of Surgeons, Boston, Mass. Cloth. Price, $2.00. Pp. 93, with 24 illustrations. New York: Paul B. Hoeber, Inc., 1925.

This book is a reprint, with corrections of an article published in the February, 1925, number of the *American Journal of Roentgenology and Radium Therapy*. The author aims to present to the medical profession, and especially to those interested in bone tumors, a classification of such tumors with a

nomenclature suitable to clinicians, roentgenologists and pathologists, thereby making possible a more common understanding of bone tumors. The classification herein proposed, and one adopted jointly by the committee of registry of bone sarcoma, consisting of the author and Drs. Ewing and Bloodgood, and the committee of the Clinical Pathological Association, composed of Drs. MacCarty, Sondern, St. George and Bell, is one of eight divisions. These divisions are metastatic tumors, periosteal fibrosarcoma, osteogenic tumors (benign and malignant), inflammatory conditions, benign giant cell tumors, angiomas (benign and malignant), Ewing's tumor and myeloma. Each division, so far as is possible, the author defines and interprets on a clinical, anatomic and roentgenologic basis, with splendid illustrations of the latter two; he also points out the difficulty encountered in classifying certain tumors, concerning which there is as yet no uniformity of opinion. In this regard the author invites constructive criticism from authorities on bone tumors, with a view of ultimately arriving at a standard classification. Attention is also directed by the author to the matter of submitting bone tumor cases to the Registry for registration and the attendant details necessary for such registration; to this end he has supplemented a list of descriptive adjectives and prefixes used in the literature for bone tumors and some of the cases already registered. He concludes with an appeal to surgeons, roentgenologists and pathologists for a hearty cooperation in making the Registry a basis for teaching in our medical schools and an internationally recognized institution.

THE CHILD, HIS CARE AND FEEDING, FROM BIRTH TO SCHOOL AGE. By FRITZ STIRNIMANN, M.D. Pp. 209. Stans, Switzerland: Hans von Matt, August 1925.

This book on the care and feeding of children from birth to school age differs in no essential feature from other books of its type. In the place of the calory or nem, the gram of starch unit representing four calories, is introduced in the feeding and is used in the tables. There seems to be no particular reason for introducing this new unit. To assist the reader, the principal terms used by the author are arranged alphabetically with their translation into French, English and Italian at the end of the book.

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